Electromagnetic Fields:
Effects on Waking, Sleep and Cognitive Performance

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by

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for Malte

for my parents

„Man muss noch Chaos in sich haben,
um einen tanzenden Stern gebären zu können"

(aus: Friedrich Nietzsche, Also sprach Zarathustra)

PREFACE

The scientific research reported in this thesis was performed at the Institute of Pharmacology and Toxicology at the University of Zürich. I am indebted to Professor René Hirsig and Professor Alexander A. Borbély for giving me the opportunity to accomplish my doctoral work in the Section of Psychopharmacology and Sleep Research, and especially to Dr. Peter Achermann for his constant supervision, support and guidance during my dissertation research. Without his expertise and patience, the work presented here would not have been possible. I am grateful to Professor Alexander A. Borbély and Dr. Hans-Peter Landolt for their helpful comments on data analyses and manuscripts and for being my co-examiners. Moreover, I would like to thank Dr. Julie Gottselig for her generous support with the programming of the cognitive tasks and her precious comments on the design of the first experiment (chapter 3.1). I owe a heartfelt thank you to the entire human laboratory for their kind assistance during the first two experiments (chapter 3.1 and chapter 3.2) and to Dr. Sonja Negovetic, Nora Fischer (b. Burgermeister) and Eveline Honegger for their indispensable help with study III (chapter 3.3). Special thanks to all the subjects who participated in the experiments and made this work possible. Thanks to Dr. Roland Dürr, Karl Wüthrich, Harald Osswald and Peter Sepan for their technical support. Yvonne Maeder for her administrative help. I gratefully acknowledge the efforts of the IT'IS Foundation (Professor Niels Kuster, Dr. Jürgen Schuderer, Veronica Berdiñas, Dr. Urs Lott, Sven Ebert, Denis Spät and Sven Kühn) for the provision of the exposure setup, dosimetry assessment and support with the exposure equipment. Moreover, I am deeply thankful for the intense collaboration with Dr. Martin Röösli and Dr. Anke Huss of the University of Bern during the third project (chapter 3.3).

Most notably, I would like to thank Julia Rétey for her company and humor during the last four years. Feli, Nadia, Julia, Cris and Claudia for one hot meal per week. Simon and Reto for relaxed living. Tom and Thieu for hilarious evenings and an unforgettable period of life. Wes for far-reaching discussions across the Atlantic. Inge for everlasting warm feet. Birte, Leylâ, Netti, Tanja, Isa and Schappi for being who they are, no matter where they are. Martina and Nina for insistent visiting. Hanna for her constant smile. Christoph for healthy criticism once in a while. Petra, Frank and Sven for going with me through some difficult times. Soo-Yun and Olli for standing by me all my life. And finally, yet importantly, all my family and friends for being an inexhaustible source of energy and motivation.

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SUMMARY

The number of mobile phone users is steadily increasing and there is a rising concern about possible adverse health effects of radio frequency electromagnetic fields (RF EMF). In view of these developments there is an urgent need for investigating the effects of mobile communication systems on brain functioning. RF EMF are absorbed in the body. Since at the usual field strength the thermal effect of RF EMF in the exposed tissue is negligible, the focus of research is on potential non-thermal effects. An extensive literature overview (chapter 2) revealed that reports of RF EMF induced effects on brain electrophysiology contain more consistent results than those on cognitive performance.

The experimental work summarized in this thesis focused on effects of short-term RF EMF exposure on various aspects of waking and sleep. In the first study (chapter 3.1), the properties of RF EMF were varied. In different experimental sessions, subjects were exposed for 30 min to a pulse-modulated signal (PM) and a continuous-wave signal (CW; carrier frequency only). Compared to sham exposure, PM reduced reaction speed in a working memory task (1- and 2-back task) and increased accuracy in the high-memory load portion of the task (3-back task). PM affected spectral power in the waking EEG: the values in the 10.5 - 11 Hz range were increased 30 min after exposure, and at 12 Hz they were reduced 60 min after exposure. CW had no effect on cognitive performance and alpha activity. In the second study (chapter 3.2), the dose-response relationship after pulse-modulated RF EMF exposure was investigated by varying signal intensity in three experimental sessions (RF EMF with a specific absorption rate (SAR) of 0.2 W/kg and 5 W/kg, and sham control). The reaction speed in the cognitive tasks performed during the 30-min exposure tended to decelerate with increasing field intensity. No dose-dependent effect on accuracy was observed. In subsequent nighttime sleep, spectral EEG power in stage 2 showed a dose-dependent increase, whereas sleep architecture was not affected. In the third study (chapter 3.3), subjects were exposed for 45 min to a Universal Mobile Telecommunication System (UMTS) base station-like signal at two different electric field strengths (1 V/m, 10 V/m) and a sham control to examine the effect on well-being and cognitive performance. The peak spatial SAR in brain tissue was considerably smaller than during use of a mobile phone. Persons with and without self-reported sensitivity to RF EMF were tested. In neither group, well-being and perceived field strength were associated with the actual exposure level. No consistent condition-induced changes in cognitive performance were observed.

In summary, the present thesis provides further evidence that RF EMF exposure can alter brain physiology. The results of the first study demonstrate that pulse modulation of the RF EMF signal is necessary to induce EEG changes in waking. The findings of the second study demonstrate that RF EMF exposure may affect brain activity in a dose-dependent manner. The third study shows that short-term exposure to a base station-like UMTS signal does not affect well-being and cognition. The issue of possible adverse health effects of RF EMF was not addressed in these studies.

ZUSAMMENFASSUNG

Die Anzahl von Mobiltelefonnutzern steigt stetig an und geht mit einer wachsenden Besorgnis bezüglich negativer gesundheitlicher Auswirkungen von elektromagnetischen Feldern im Radiofrequenzbereich (RF EMF) einher. In Anbetracht dieser Entwicklung ist die Untersuchung der Effekte des Mobilfunks auf die Hirnfunktion dringend notwendig. RF EMF werden vom Körper absorbiert. Da thermische Effekte auf das Körpergewebe bei herkömmlichen Feldstärken vernachlässigbar sind, liegt der Forschungsschwerpunkt auf der Untersuchung möglicher nicht-thermischer Effekte. Ein ausführlicher Literaturüberblick (Kapitel 2) zeigte, dass Befunde bezüglich der Beeinflussung der Hirnelektrophysiologie durch RF EMF konsistentere Resultate aufwiesen als Befunde bezüglich kognitiver Leistungen.

Die in dieser Dissertation zusammengefassten experimentellen Arbeiten behandeln die Effekte kurzzeitiger RF EMF Expositionen auf verschiedene Aspekte des Wach- und Schlafzustandes. In der ersten Studie (Kapitel 3.1) wurden die Eigenschaften der RF EMF (Exposition) variiert. In verschiedenen experimentellen Sitzungen wurden die Versuchspersonen je 30 Min lang einem pulsmodulierten (PM) bzw. einem kontinuierlichen Signal (CW; nur die Trägerfrequenz) ausgesetzt. Verglichen mit der Kontrollbedingung (kein Feld) führte das PM EMF zu einer verringerten Reaktionsgeschwindigkeit in einer Aufgabe zum Arbeitsgedächtnis (1-back und 2-back Test), und zu einer erhöhten Genauigkeit auf der höchsten Schwierigkeitsstufe derselben Aufgabe (3-back Test). Das pulsmodulierte EMF beeinflusste die spektrale Leistung im Wach-EEG: die Werte im Frequenzbereich von 10.5 bis 11 Hz waren 30 Min nach der Exposition erhöht und bei 12 Hz 60 Min nach der Exposition reduziert. Das kontinuierliche Signal (CW) hatte keinen Einfluss auf die kognitive Leistung und die Alpha-Aktivität. In der zweiten Studie (Kapitel 3.2) wurde die Dosis-Wirkungs-Beziehung nach pulsmodulierter RF EMF Exposition untersucht, indem die Signalintensität in den drei Versuchsbedingungen variiert wurde (RF EMF mit einer spezifischen Absorptionsrate (SAR) von 0.2 W/kg und 5 W/kg, sowie eine Kontrollbedingung ohne Feld). Die kognitiven Tests wurden während der 30-minütigen Exposition durchgeführt und es zeigte sich, dass die Reaktionsgeschwindigkeit tendenziell mit zunehmender Feldintensität abnahm. Auf die Genauigkeit konnte kein dosisabhängiger Effekt festgestellt werden. Im nachfolgenden Nachtschlaf war die spektrale Leistung im Spindelbereich des Schlafstadiums 2 dosisabhängig erhöht, während die Schlafarchitektur unbeeinflusst blieb. In der dritten Studie (Kapitel 3.3) wurden die

Versuchspersonen 45 Min lang einem Universal Mobile Telecommunication System (UMTS) Basisstationssignal mit zwei unterschiedlichen Feldstärken (1 V/m, 10 V/m) und einer Kontrollbedingung ausgesetzt, um den Effekt auf Wohlbefinden und kognitive Leistungsfähigkeit zu untersuchen. Der maximale SAR-Wert im Gehirn war bedeutend kleiner als während der Benutzung eines Mobiltelefons. Es wurden Personen untersucht, die sich in Bezug auf RF EMF subjektiv als sensitiv bzw. nichtsensitiv einschätzten. In keiner der beiden Personengruppen standen das Wohlbefinden und die wahrgenommene Feldstärke mit der realen Expositionsbedingung in Zusammenhang. Es konnten keine konsistenten, expositionsbedingten Veränderungen der kognitiven Leistungen beobachtet werden.

Zusammengefasst liefert diese Dissertation weitere Hinweise darauf, dass RF EMF die Hirnphysiologie beeinflussen kann. Die Resultate der ersten Studie zeigen, dass die Pulsmodulation des RF EMF Signals nötig ist, um EEG-Veränderungen im Wachzustand herbeizuführen. Die Befunde der zweiten Studie belegen, dass RF EMF die Gehirnaktivität in einer dosisabhängigen Weise beeinflussen können. Die dritte Studie demonstriert, dass die kurzfristige Exposition mit einem basisstationsähnlichen UMTS Signal keinen Einfluss auf Wohlbefinden und Kognition hat. Die Frage nach möglichen negativen gesundheitlichen Auswirkungen von RF EMF wurde in diesen Studien nicht untersucht.

ABBREVIATIONS

BCCH	Broadcast control channel
BL	Baseline
BMI	Body mass index
BP	Bereitschaftspotential
BQW	Bern questionnaire on well-being
CDMA	Code division multiple access
CNV	Contingent negative variation
CRT	Two-choice reaction time task
CW EMF	Continuous-wave electromagnetic field
DTX	Discontinuous transmission
ECG	Electrocardiogram
EEG	Electroencephalogram
E-field	Electric field
EHS	Electromagnetic hypersensitivity
EMF	Electromagnetic field
EMG	Electromyogram
EOG	Electrooculogram
EPSP	Excitatory postsynaptic potential
ERD	Event related desynchronization
ERP	Event related potentials
ERS	Event related synchronization
FDD	Frequency division duplex
FDMA	Frequency division multiple access
FFT	Fast fourier transform
GABA	Gamma-amino-butyric-acid
GSM	Global system for mobile communication
H-field	Magnetic field
IPSP	Inhibitory postsynaptic potential
J	Current density
LEET	Low energy emission therapy
MEG	Magnetencephalography
N-back	N-back task
NMDA	N-methyl-d-aspartat

NMT	Nordic mobile telephone
non-REM sleep	non-Rapid eye movement sleep
rCBF	Regional cerebral blood flow
PCN	Personal communication network phone
PET	Positron emission tomography
PM EMF	Pulse-modulated electromagnetic field
pp TMS	Paired pulse transcranial magnetic stimulation
psSAR	Peak spatial specific absorption rate
QCD	Questionnaire on current disposition
QCD_{diff}	Difference between post and preexperimental scores of QCD
QCD_{post}	Postexperimental scores of QCD
QOF	Self-designed questionnaire to assess other factors potentially related to well-being
REMs	Rapid eye movements
REM sleep	Rapid eye movement sleep
RF EMF	Radio frequency electromagnetic field(s)
SACCH	Slow associated control channel
SAR	Specific absorption rate
SEP	Somatosensory evoked potentials
SFA	Sigma frequency activity
SRT	Simple reaction time task
SWA	Slow wave activity
SWS	Slow wave sleep
TDD	Time division duplex
TDMA	Time division multiplex access
TMS	Transcranial magnetic stimulation
TNO	TNO Physics and Electronics Laboratory
TNO-Q	Quality-of-life questionnaire
UMTS	Universal mobile telecommunication system
UTRA	UMTS terrestrial radio access
VMT	Visual monitoring task
VSAT	Visual selective attention task

THEORETICAL PART

1 INTRODUCTION

Wakefulness and Sleep

1.1 Basic Principles of the Electroencephalogram

The electrical activity of the brain induces alternating electrical potentials at the scalp surface which can be recorded noninvasively with macroelectrodes. This type of recording is called *Electroencephalogram* (EEG). As this method is based upon the assessment of potential differences, at least two electrodes are needed, namely an active electrode and a reference electrode. Usually, numerous active electrodes are placed over frontal, temporal and occipital regions on the scalp at well defined, standardized distances ("10-20 system", referring to 10% and 20% inter-electrode distance, Jasper 1958). Potential differences can be calculated between an active and a reference electrode as well as between two active electrodes (Kandel et al. 2000). The activity of a single neuron produces too little electrical current to be recordable on the scalp surface. The potential differences of the EEG arise from highly synchronized postsynaptic field potentials generated by large assemblies of pyramidal cells in cortical lamina II, III and V. They are organized parallel to each other and their apical dendrites reach into lamina I, showing a predominant perpendicular orientation to the cortex. Pyramidal neurons are excitatory cells and supposed to act via the neurotransmitter glutamate (Kandel et al. 2000). The apical excitatory postsynaptic potentials (EPSPs) result in sodium influx into the cell and a proximal potassium efflux out of the cell. Whereas the corresponding intracellular currents form the basis of magnetencephalography (MEG), the extracellular currents are the basis of the EEG signal. Each pyramidal cell acts as a radially oriented dipole. The orientation of the dipole reverses when most of the input at the dendrites is inhibitory. Due to a high conductive periphery (cerebrospinal fluid, meninges, scalp) the potentials can be recorded with surface

electrodes and relative to a reference location, comprising frequencies about 1-50 Hz and amplitudes between 20-100 μV (Kandel et al. 2000).

1.2 The Waking Electroencephalogram

Hans Berger (1873-1941) is generally considered to be the discoverer of the human EEG (Berger 1929). The waking EEG activity comprises a large frequency range which is traditionally subdivided into several frequency bands: theta (4-7.5 Hz), alpha (8-13 Hz), beta (around 14-30 Hz), and gamma (> 30 Hz) (Niedermeyer 2005). The frequency bands (i.e., the lower and upper limits of the spectrum) are not well defined and may differ considerably in the literature.

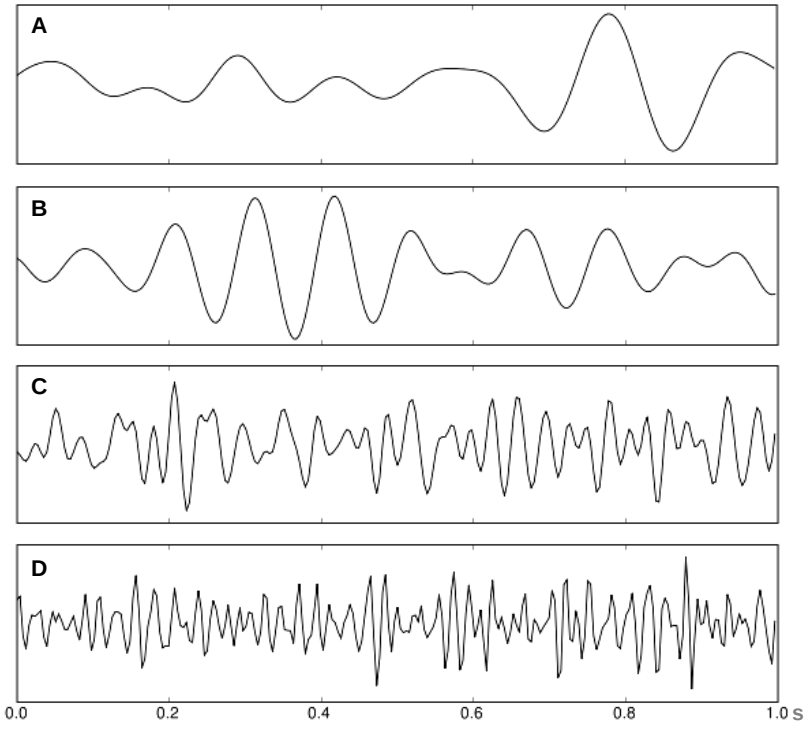

Figure 1: *Different patterns of electrical brain activity are measured by the EEG in waking. 1 s samples of the classical frequency bands are illustrated:* ***A.*** *theta (4-7.5 Hz),* ***B.*** *alpha (8-13 Hz),* ***C.*** *beta (~ 14-30 Hz)* ***D.*** *gamma (> 30 Hz) (adapted from* Hugo Gamboa, Wikimedia 2005*).*

1.2.1 Alpha Activity

Starting in 1924, Berger's studies in neurologic patients as well as in his own son resulted in the first description of the *alpha rhythm* (Berger 1929). In general, this rhythm dominates the waking EEG in relaxed wakefulness in a subset of human subjects and is characterized by sinusoidal waveforms of approximately 10 Hz (e.g., Klimesch 1999). The frequency is not stable but develops over childhood showing a gradual increase over about 10-15 years (i.e., 4 months: ~ 4 Hz; 12 months: ~ 6 Hz; 36 months: ~ 8 Hz). The frequency reaches a mean of about 10 Hz at the age of about 10 years, followed by a decline with further aging (Klimesch 1999; Niedermeyer 2005). According to the International Federation of Clinical Neurophysiology, alpha activity is defined as a "*rhythm at 8-13 Hz occurring during wakefulness over the posterior regions of the head, generally with maximum amplitudes over the occipital areas. Amplitude varies but is mostly below 50 μV in the adult. Best seen with the eyes closed and during physical relaxation and relative mental inactivity. Blocked or attenuated by attention, especially visual, and mental effort*" (Noachtar et al. 1999). Although it is most pronounced over posterior parts of the head, it may also extend to central areas, where it has to be differentiated from the *mu rhythm* (or *rolandic alpha* (~ 9 Hz), Gastaut 1952). This rhythm, which is not detectable in every human adult, appears mainly over the motor cortex and adjacent somatosensory areas and is suppressed during motor related tasks. Alpha and mu rhythms clearly reflect independent processes, as eye opening causes an alpha block but leaves the mu rhythm unaffected (Klimesch 1999; Niedermeyer 2005). The so called "squeak effect" describes a short increase of the alpha frequency immediately after eye closure (after Storm van Leeuwen and Bekkering 1958). Eye opening may lead to an attenuation of alpha activity with amplitude reduction, but also to a complete alpha block, already described by Berger (1929). The attenuation due to external sensory stimulation or mental efforts is usually not as strong as the blocking effect due to opening of the eyes (Niedermeyer et al. 1989). Generally, alpha activity of lower frequencies is found at anterior recording sites and alpha activity of higher frequencies is found at posterior recording sites (Klimesch 1999). Moreover, it was reported that higher power densities (spectral density of the wave per unit frequency) are found in the right hemisphere (e.g., Wieneke et al. 1980). Not every human being, however, expresses alpha activity. Alpha traits seem to be at least partially genetically transmitted and altogether four alpha-subtypes have been proposed: dominant alpha (~ 24% of the healthy adults), subdominant alpha (~ 32%), mixed alpha (~ 26%) and

rare alpha (~ 18%, Davis and Davis 1936). A twin study (213 twin pairs) on the genetic and environmental contributions to individual differences in CNS functioning suggested an averaged heritability for alpha frequencies of ~ 89% (van Beijsterveldt et al. 1996).

Early findings on alpha activity and cognitive performance suggest that a high alpha frequency is associated with fast reaction times, whereas a low frequency is associated with slow reaction times (e.g., Surwillo 1961). Data of Klimesch (1997) indicate that alpha frequencies of good memory performers are about 1 Hz higher than those of bad performers. But alpha frequencies and amplitudes may not only show high interindividual, but also high intraindividual variation dependent on the condition. In this context it has been suggested that alpha activity may be an indicator of cognitive and memory performance as with increasing task demands theta power synchronizes (increases), whereas alpha power desynchronizes (decreases, Klimesch 1997). This alpha desynchronization, however, seems to be a local phenomenon occurring over task relevant brain areas only. In contrast, task irrelevant regions show a pronounced synchronization (Klimesch et al. 1999).

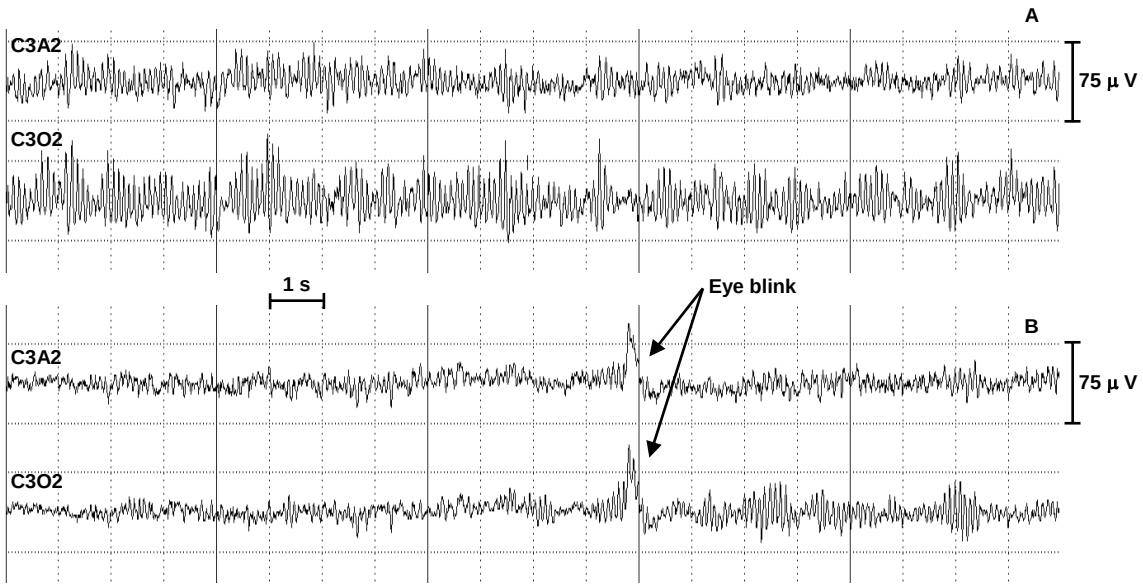

Figure 2: *20 s wake-EEG recording in a 24 year old male subject. Two different derivations are illustrated (C3A2, C3O2).* ***A:*** *Alpha activity (8-13 Hz) in the eyes closed condition. Note that alpha is more pronounced in the posterior part of the head (C3O2) compared to C3A2.* ***B:*** *Alpha activity is attenuated or even blocked in the eyes open condition. Note the low voltage, fast activity and the reoccurrence especially of posterior alpha rhythm after eye opening. Also note typical artifacts due to eye blinking.*

1.2.2 Event Related Potentials

Whereas the spontaneous EEG is generally used to quantify the global functional state of the brain, event related potential (ERP) studies can assess cognitive processing while the subject is involved in cognitive tasks. The ERPs reflect changes in the potential difference ranging between 2-20 μV due to a sudden or expected stimulus (e.g., a tone). Yet, to enhance the signal-to-noise-ratio in the EEG recording, the event related electric activity has to be identified from the background noise of spontaneous activity by specific time-locked averaging techniques (Altenmüller et al. 2005; Lopes da Silva 2005). The resulting characteristic wave shape is analyzed in terms of peak latencies (time point of max. positive or negative voltage after stimulus presentation) and amplitudes (generally measured peak to peak). These components are usually labeled according to their polarity (positive (P) or negative (N), relative to the reference electrode) as well as according to their characteristic peak latencies (e.g., P300 for a positive peak at approximately 300 ms after stimulus onset), their actual peak latencies in a specific environment (e.g., N148, P135) or their appearance (e.g., N1, P1, P2, Altenmüller et al. 2005). The early components of the evoked potential waveform are dependent on physical stimulus characteristics (e.g., loudness of a tone) and are therefore referred to as *exogenous* ERPs. They are distinguished from *endogenous* ERPs, which seem to vary with a variety of psychological variables (e.g., expectancy of a stimulus) and occupy the later portions of the ERP (> 100 ms, Altenmüller et al. 2005).

One way to assess stimulus-related responses of different EEG frequency bands includes the so called *event related synchronization* (ERS) and *desynchronization* (ERD) analysis of the EEG. Whereas the ERS describes an increase of the oscillatory activity of alpha or beta power occurring related to an event in the form of bursts or spindles (Pfurtscheller 1991), the ERD describes the reverse process, namely a phasic and regional specific relative reduction or even blockade of these frequency bands (Pfurtscheller and Aranibar 1977).

1.3 The Sleep Electroencephalogram

Originally focusing on the awake brain, Hans Berger was also the first to show sleep spindle activity (Berger 1929). Until today the continuous recording of the brain's electrical activity is still the gold standard method in modern sleep research. In humans, besides the EEG, eye movements (electrooculogram; EOG) as well as chin muscle tone (electromyogram; EMG) are generally recorded simultaneously in order to enable the precise differentiation between the basic sleep states, rapid eye movement (REM) sleep and non-rapid eye movement (non-REM) sleep. Both states alternate throughout the night, forming 4-7 recurring cycles of about 90-110 min in length. Non-REM sleep is subdivided into four stages (Dement and Kleitman 1957; Rechtschaffen and Kales 1968). Based on the standard criteria by Rechtschaffen and Kales (1968), stage 1 constitutes an intermittent stage between waking and sleep and includes an irregular low voltage, mixed frequency EEG. *Vertex sharp waves* (up to 200 μV peak to peak) and rhythmic *theta waves* (50-75 μV peak to peak) are a common feature of the onset of stage 1 sleep, which are mainly localized at the vertex region and therefore may not be observed in every EEG derivation. Especially following wakefulness, stage 1 is characterized by slow eye movements. Tonic EMG levels are generally below those of relaxed wakefulness. *Sleep spindles* (~ 12-14 Hz) and *K-complexes* on the background of low voltage, mixed frequency EEG activity are the most prominent features of stage 2 sleep. The two phenomena can occur together with the sleep spindle on the trailing portion of the K-complex. By definition, sleep spindles must comprise six or seven distinct waves within a half-second period. The K-complex itself constitutes a negative sharp wave followed immediately by a slower positive component, also with a duration of at least half a second. Usually, the tonic EMG is relatively low. Stage 3 and 4 contain moderate (≥ 20-50%) and large amounts (> 50%) of *delta waves* (~ 1-4 Hz) with a high amplitude (> 75 μV peak to peak), respectively, and are hence generally also referred to as *slow wave sleep* (SWS). Sleep spindles may or may not occur in SWS and the muscle tone is generally low. REM sleep on the other hand comprises a relatively low voltage, mixed frequency EEG in conjunction with episodic rapid eye movements (REMs) and low amplitude EMG. S*aw-tooth waves* are a common feature in REM sleep frequently occurring simultaneously with bursts of REMs.

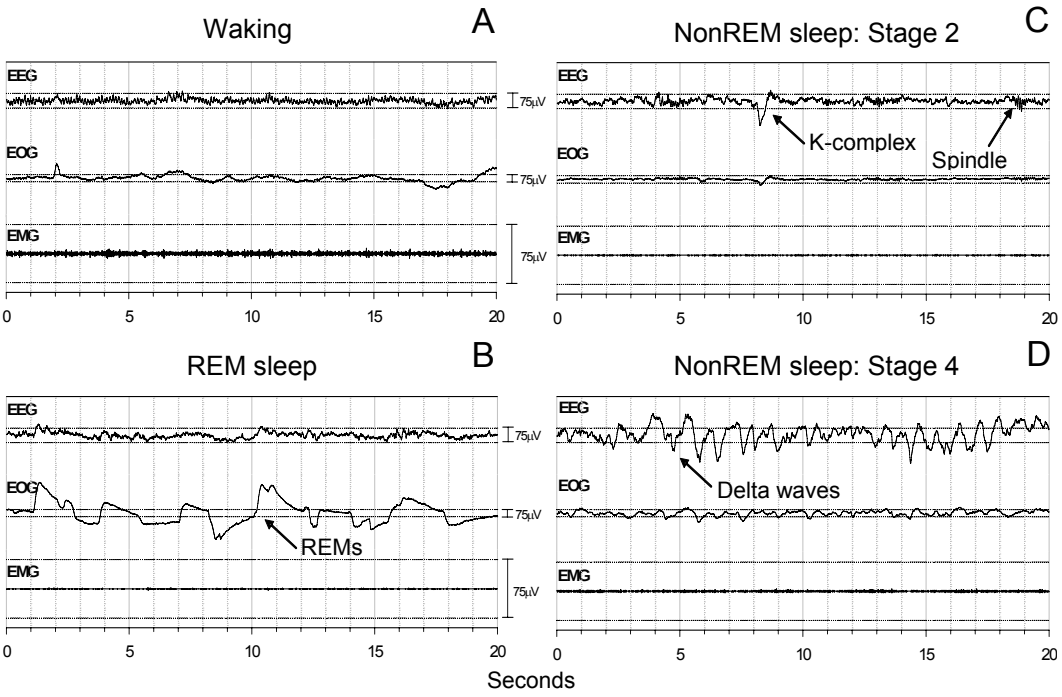

Figure 3: *EEG, EOG and EMG signals in waking and sleep.* ***A****: The waking state is characterized by alpha activity (~ 8-13 Hz) and/or low voltage, mixed frequency EEG (see also Figure 2). Generally, the muscle tone is high (EMG) and rapid eye movements and/or eye blinks occur (EOG).* ***B****: REM sleep is characterized by low voltage, mixed-frequency EEG, rapid eye movements (REMs) and low muscle tone.* ***C****: Non-REM sleep stage 2 constitutes of a low voltage, mixed frequency EEG and includes K-complexes and sleep spindles (~ 12-14 Hz).* ***D****: Non-REM sleep stages 3 and 4 are dominated by EEG delta waves (~ 1-4 Hz) and thus referred to as slow wave sleep.*

1.3.1 Sleep Spindles

The name for this type of oscillations is derived from its spindle-like appearance with its waxing and waning amplitude. Although first observed by Hans Berger (Berger 1929), the term was coined by Loomis and co-workers in 1935 (Loomis et al. 1935). According to the International Federation of Clinical Neurophysiology, sleep spindles are defined as "*bursts at 11-15 Hz but mostly at 12-14 Hz generally diffuse but of higher voltage over the central regions of the head, occurring during sleep. Amplitude varies but is mostly below 50 μV in the adult*" (Noachtar et al. 1999). In humans, sleep spindle frequency activity (SFA), also known as *sigma activity*, occurs rhythmically every 3 to 6 s with

duration of at least 0.5 s (Nicolas et al. 2001; Rechtschaffen and Kales 1968). It is generally observed in low voltage background EEG but may also be present e.g., superimposed to delta activity (Rechtschaffen and Kales 1968). Sleep spindles in the 13-14 Hz band show high intrahemispheric and interhemispheric coherence (Achermann and Borbély 1998a; Achermann and Borbély 1998b). Two independent types of SFA have been described. Thus, “slow” spindles (~ 12 Hz) have been distinguished from “fast” spindles (~ 14 Hz) with the former being localized more frontally, the latter being localized more parietally (e.g., Jobert et al. 1992; Werth et al. 1997). Low and fast spindles exhibit opposite circadian variations (12.25-13 Hz, 14.25-15 Hz, Aeschbach et al. 1997) and are differently affected by age (Landolt et al. 1996).

Sleep spindles usually develop before three months of age in humans (e.g., Crowell et al. 1982; Ellingson 1982). A longitudinal study by Louis et al. (1992) revealed a rapid increase in six parameters (density, duration, frequency, amplitude, asymmetry and asynchrony) with respect to spindle ontogenesis in infants between 1.5 and 3 months of age. In line with this finding, Jenni et al. (2004) reported an increased peak frequency from 12.6 Hz (2 months) up to 13.1 Hz (9 months of age). The percentage of spindle activity (average number and length of sleep spindles in stage 2 sleep) in the 11.5-14 Hz range seems to reach its maximum between 4 and 6 months of age (Tanguay et al. 1975). Followed by minimal values at the age of about 27 months, the percentage remains stable up to 54 months and then starts to rise again. Despite an increasing spindle frequency, most spindle variables are attenuated with increasing age, mainly in the first four decades of aging: spindles may slow down, decrease in number and density, exhibit a lower amplitude and a shorter duration in old compared to young adults (e.g., Nicolas et al. 2001; Principe and Smith 1982). Accordingly, an age dependent decrease of spectral power density in the sigma frequency range has been described (Dijk et al. 1989).

Spindle density appears to be a fairly stable individual characteristic (Gaillard and Blois 1981). In line with this, Werth et al. (1997) reported only little variation with respect to the peak frequency between nights or over consecutive non-REM sleep episodes in individuals, although interindividual variation was large. Contrary to slow wave activity throughout the night, a progressive increase in sigma activity has been observed across consecutive sleep cycles during nighttime sleep (Aeschbach and Borbély 1993). This effect, however, seems to become less prominent with age (Landolt et al. 1996) and can not be observed in infants (Jenni et al. 2004). Moreover, the U-shaped time course of

sigma frequency activity within cycles occurs in adults (e.g., Aeschbach and Borbély 1993; Landolt et al. 1996), but not in infants (Jenni et al. 2004). Werth et al. (1997) reported a declining trend of spindle frequency power over consecutive non-REM sleep episodes in the low range of SFA (12 Hz) but an increasing trend in the high range (14 Hz).

A variety of benzodiazepine hypnotics acting as agonists at the $GABA_A$-benzodiazepine receptor complex are known to enhance SFA and to decrease slow wave activity (SWA: EEG power density between 0.75 and 4.5 Hz; Aeschbach et al. 1994b; Hirshkowitz et al. 1982). Aeschbach et al. (1994a) reported reduced EEG power densities in non-REM sleep in the frequency range of 1.25-10 Hz (~ 20-25% decrease) and enhanced EEG power densities in the frequency range of 12.25-13 Hz (~ 25-30% increase) after 0.25 mg triazolam. Total sleep deprivation, on the other hand, leads to reduced sigma activity and spindle density during recovery nights, suggesting an inverse relation between sigma and slow wave activity within non-REM sleep (e.g., Dijk et al. 1993; Uchida et al. 1991). Besides the homeostatic influences, SFA is also modulated by circadian factors with a maximum appearing in the initial part of the habitual sleep episode (Dijk and Czeisler 1995a). Melatonin was reported to enhance EEG power density in the frequency range between 13.75-14 Hz (Dijk et al. 1995b).

1.4 The Mechanisms Underlying the EEG Patterns of Sleep and Wakefulness

For a long time, sleep was considered to be a passive state in the absence of waking. In 1915, Constantin von Economo (1876-1931) observed that patients who had been infected with an influenza virus showed excessive sleepiness, a condition designated as *encephalitis lethargica* (von Economo 1917). This condition was associated with inflammatory changes in the tegmentum of the midbrain and the basal ganglia. In contrast, patients with damage to the anterior hypothalamus were unable to fall sleep. This suggested that both sleep and waking are active processes controlled by specific structures of the brain. Further evidence was obtained by Moruzzi and Magoun (1949) as well as Hess (1950) who observed that the stimulation of the brainstem reticular formation and the thalamus, respectively, can trigger EEG patterns in the cortex characteristic of waking or sleep.

Wakefulness and sleep are two distinct states which can be clearly differentiated based on EEG recordings. Whereas faster patterns are the hallmark of the aroused brain, neural activity changes remarkably at the transition to non-REM sleep, resulting in increasing large-amplitude and low-frequency oscillations. The underlying mechanism responsible for these oscillatory changes involves the thalamus as well as the cerebral cortex, which are linked by reciprocal projections (Steriade et al. 1993a).

In non-REM sleep, thalamocortical activity exhibits synchronized rhythmic activity characterized by a burst-pause firing pattern. Three major oscillations can be observed: sleep spindles (12-14 Hz), delta waves (1-4 Hz) and slow oscillations (< 1 Hz). Sleep spindles arise from changing activity patterns in interconnected glutamatergic thalamocortical and GABAergic reticular neurons at a membrane potential around −60 mV. A reduced intracellular Ca^{2+} concentration promotes a burst of spikes in the thalamocortical cell, exciting reticular thalamic neurons which in turn hyperpolarize and induce rhythmic inhibitory postsynaptic potentials (IPSPs) in target thalamocortical neurons. The IPSPs de-inactivate a transient low threshold Ca^{2+} current and the spindle is terminated by an intracellular increase of Ca^{2+} (Steriade et al. 1993a; Steriade 2003a). Due to the prolonged hyperpolarization below ~ −70 mV, spindle oscillations are more and more reduced and replaced by delta waves (1-4 Hz), the main source of slow wave activity (Steriade 2003a; Steriade and Timofeev 2003b). Contrary to the generation of sleep spindles, delta oscillations reflect an intrinsic oscillation of thalamocortical neurons, which is based on the interplay between two inward currents, a hyperpolarization-activated cation current and a transient low-threshold Ca^{2+} current. Slow wave activity is regarded as the EEG marker of sleep homeostasis, showing an exponential decay in the course of the night (Borbély et al. 1981). Slow oscillations (< 1 Hz) were observed in intracellular studies as well as in EEG recordings (Achermann and Borbély 1997; Steriade et al. 1993b) and are generally considered as distinct from slow wave activity. This assumption is supported e.g., by Achermann and Borbély (1997) who did not observe a reduction in slow oscillations (0.55-0.95 Hz range) from the first to the second non-REM episode of a night. The cortical nature of slow oscillations was demonstrated in several studies (e.g., Steriade et al. 1993b) and comprises a slow NMDA-mediated depolarizing phase (“up-state”) during which neurons fire at high rates, followed by a long-lasting hyperpolarization (“down-state”) lacking neuronal activity (Steriade et al. 1993b; Steriade and Timofeev 2003b).

Besides the synchronized rhythmic activity during sleep, thalamocortical activity exhibits a second state of tonic activity characterized by a single spike firing pattern during waking and REM sleep. Due to an increased firing rate of cholinergic neurons arising in the mesopontine nuclei, thalamocortical cells are excited and become less hyperpolarized at the transition from non-REM to REM sleep (Steriade et al. 1990). This leads to a continuous reduction of low-frequency rhythms as well as a promotion of high-frequency oscillations in thalamocortical systems during REM sleep similar to the waking state. Yet, wakefulness is produced by additional release of acetylcholine, norepinephrine, serotonin and histamine within the ascending activation system.

1.5 Spectral Analysis

Generally, sleep stages of human recordings are visually scored. Spectral analysis is a mathematical approach to quantify the EEG. Its purpose is the decomposition of signals (e.g., the EEG) into its constituting frequency components. A commonly used method is the fast Fourier transform (FFT, Cooley and Tukey 1965). Prerequisites are a sufficiently high sampling rate (sampling theorem; Nyquest frequency) and the stationarity of the signal (i.e., statistical properties do not change over time). To meet the sampling theorem, appropriate anti-aliasing low-pass filters have to be applied. The sleep EEG is a non-stationary signal with typical changes as a function of the non-REM-REM sleep cycle. Nevertheless, by selecting short epochs in which the parameters of interest vary little, the requirements for stationarity may be fulfilled (quasi stationarity). The power density spectrum or power spectrum displays the distribution of power or variance over the elementary frequency components of the signal. Thus, rhythmic activity in the EEG is reflected by peaks in the power spectrum. The frequency resolution is the inverse of the length of the analyzed epoch. In case of the frequently used FFT of 4-s EEG epochs, for example, this results in a resolution of 0.25 Hz. EEG power density spectra are expressed as power per bandwidth (for example μV^2/Hz). In the EEG power spectrum of awake, healthy human volunteers a dominant peak appears in the alpha frequency range (~ 8-13 Hz). In the all night EEG spectrum, power density values decrease with increasing frequency, exhibiting dominant peaks at around 1-2 Hz (delta), 5-8 Hz (theta) and 12-14 Hz (sleep spindle range). Absolute spectral power is strongly affected by e.g., the thickness of the skull or age (Klimesch 1999).

1.6 Mobile Communication in the Electromagnetic Spectrum

The electromagnetic spectrum can be divided according to the photon energy or equivalently according to wavelength (λ) or frequency (f). The spectrum has two important divisions: *non-ionizing* radiation (too little energy to remove electrons from atoms) and *ionizing* radiation (enough energy to remove electrons from atoms, thus creating ions). It ranges from extremely low frequencies (e.g., power lines), radiofrequency and microwave radiation (RF EMF) to infrared, ultraviolet and X-ray radiation (Moulder 1998, see Figure 4). Cellular telephony utilizes frequencies between 400 MHz – 2.3 GHz.

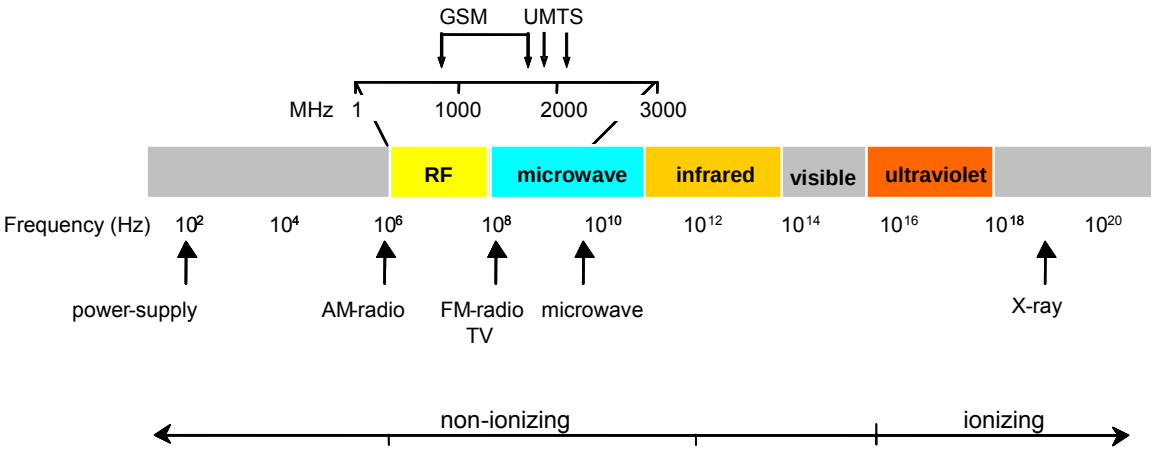

Figure 4: *The electromagnetic spectrum (adapted from Moulder 1998).*

1.7 European Land Mobile Communication Systems

1.7.1 Global System for Mobile Communication

Currently, the Global System for Mobile Communication (GSM) is the most widely used mobile voice communication system in Europe. In Europe, the system is operated in frequency bands at 900 and 1800 MHz. In order to allow access to a maximum number of users, a combination of Frequency Division Multiple Access (FDMA) and Time Division Multiplex Access (TDMA) is applied; the bands are subdivided into 200 kHz wide channels in the frequency domain and each channel is subdivided in the time domain into TDMA frames with eight communication slots of 576.9 µs duration each. The TDMA frames are then further combined in multiframes of 120 ms duration. An

active voice link of a handset (i.e., mobile telephone) occupies a single communication slot. GSM makes use of Discontinuous Transmission (DTX), a method of momentarily powering down a handset if no data needs to be transmitted (i.e., a mobile phone only transmits when the user is talking). The pulsed behavior introduces low frequency components of 217 Hz (multiples for multiple occupied slots), 8 Hz due to the frame structures and 2 Hz if DTX is present. For setting the handset power control level, the received power at the base station is typically measured over a Slow Associated Control Channel (SACCH) multiframe, which enables a power control update interval no faster than every 480 ms. The handset power control is typically implemented in 2 dB steps with a step interval of 60 ms.

The power control results in subHz frequency modulations when the phone is operated in the environment where the dominant exposure occurs at handovers during which the phone operates at full power (Wiart et al. 2000). GSM base stations continuously transmit the Broadcast Control Channel (BCCH) that is used to detect and synchronize the handset with the network.

Table 1: *Basic parameters of the Global System for Mobile Communication (GSM).*

	GSM 900		**DCS 1800 GSM**	
	Mobile phone	**Base station**	**Mobile phone**	**Base station**
European Carrier Frequency Bands (FDD)	890-915 MHz	935-960 MHz	1710-1785 MHz	1805-1880 MHz
Channel Bandwidth	200 kHz			
Channels	124		374	
Modulation	GMSK[a] (EDGE[b]: 8-PSK)			
Channel Access Method	TDMA			
Typical Maximum Peak Output Power	2 W	several hundred watts per carrier	1 W	several hundred watts per carrier
Power Control Dynamic Range	30 dB	0	30 dB	0
TDMA Frame Structure	burst: 0.577ms; TDMA frame=8 bursts=4.61 ms; multiframe=120 ms			

[a] GMSK: Gaussian Minimum Shift Keying; [b] EDGE: Enhanced Data Rates for GSM Evolution; uses 8-Phase-shift keying (8-PSK)

1.7.2 Universal Mobile Telecommunication System

The Universal Mobile Telecommunication System (UMTS) radio or air interface is known as UTRA (UMTS Terrestrial Radio Access). The air interface enables communication to take place between the handset and the base station. UMTS applies the Code Division Multiple Access method (CDMA). CDMA is a procedure in which all users on a network can operate on the same frequency. Separation of the individual communication channels is achieved using orthogonal (unambiguous) codes.

During a call, the radiated power can be adapted in both up- and downlinks. The handset is capable of changing the output power in 0.25-1.5 dB steps every 0.67 ms. The communication system architecture inherently requires that the radiated power is always only as high as is necessary to ensure a good connection. The transmitters therefore tend to operate at much lower average powers than GSM systems.

Two modes of operation are defined in the UTRA air interface: FDD (Frequency Division Duplex) mode and TDD (Time Division Duplex) mode. In FDD mode, two separate frequencies are used for a connection: one for the connection from the handset to the base station and one from the base station to the handset. Currently, FDD is the typical UMTS mode of operation. In UMTS-TDD, communication frames with a duration of 10 ms are applied whereby the frame is subdivided into 15 slots, resulting in a pulsed signal structure with a burst of 667 µs.

Table 2: *Basic parameters of the Universal Mobile Telecommunication System (UMTS).*

	Mobile phone	**Base station**
European Carrier Frequency Bands (FDD)	1920 – 1980 MHz	2110 – 2170 MHz
European Carrier Frequency Bands (TDD)	1900 - 1920 and 2010 – 2025 MHz	
Channel Bandwidth	5 MHz	
Modulation	4-PSK[a] (HSDPA/HSUPA[b] 16-QAM)	
Channel Access Method	CDMA	
Typical Maximum Peak Output Power	0.125 - 0.250 W	< 400 W
Power Control Dynamic Range	80 dB	30 dB
TDD Frame Structure	10 ms / 15 slots (asynchronously allocable)	

[a] 4-Phase-shift keying (4-PSK); [b] HSDPA/HSUPA: High Speed Downlink/Uplink Packet Access; uses 16-quadrature amplitude modulation (16-QAM)

1.7.3 Primary Safety Exposure Limits

Restrictions on electromagnetic field (EMF) exposures that are based directly on established health effects are termed basic restrictions. Depending on the frequency of the field, the physical quantities used to specify these restrictions are either the *current density* (J) or the *specific absorption rate* (SAR). The dosimetric quantities used in current guidelines (ICNIRP 1998; IEEE 2002; 2005) are J [A/m^2] for frequencies up to 10 MHz and SAR [W/kg] for the frequency range from 100 kHz to 10 GHz. J is related to the internal electric field by Ohm's law:

$$J = \sigma E$$

E [V/m] is the internal electric field, and σ [S/m] is the complex conductivity of the tissue. SAR is the ratio of the average rate of the absorbed power to the absorbing mass. It can be calculated directly from the electrical loss, which is proportional to the mean square of the locally induced electric field E:

$$SAR = \frac{\sigma E^2}{\rho} = \frac{J^2}{\sigma \rho}$$

and to a temperature increase by:

$$SAR = c\frac{dT}{dt}$$

where c [J/(kg K)] is the local specific heat capacity of the tissue, ρ [kg/m^3] is the tissue density and dT/dt [K/s] is the rate of the temperature change. This latter equation is valid only if the exposed body is in thermal equilibrium or in a steady thermal state at the beginning of the exposure, and either heat exchange processes can be neglected during the measurement interval or the processes are known to correct dT correspondingly. Current safety standards (ICNIRP 1998; IEEE 2002; 2005) for limiting EMF exposure provide maximum limits for basic restrictions for uncontrolled (general public) exposure as well as for controlled (occupational) exposure over the whole considered frequency range. The standards are ambivalent with respect to the quantity SAR. The debate among experts is whether SAR is a dosimetric quantity only relevant as a surrogate for

thermally based models of EMF interaction or whether it can describe effects in addition to those related to temperature. SAR is directly related to the induced internal electric fields (E-fields) as well as to the current density but is only in special cases directly related to the induced magnetic fields (H-fields).

1.7.4 Typical Human Exposure to Wireless Communication Devices

Exposure assessments for sources at distances larger than a few meters are based on worst-case evaluations using simplified models (Durney et al. 1997). Recently, computational electromagnetics has become sufficiently powerful to conduct detailed dosimetric analyses. However, more sophisticated evaluations are still restricted due to the small number of different human models representing different anatomies. Considerable progress has been achieved in the evaluation of near field sources such as handsets and other transmitters (Kuster and Balzano 1992; Kuster et al. 1997; Schmid et al. 1996). Standardized tests to demonstrate compliance are routinely applied (CENELEC 2001; IEEE 2002).

The daily local RF exposure of the general public has increased by several orders of magnitude with the introduction and proliferation of mobile telephony. A study regarding indoor incident field exposure from cellular base station sites was conducted by ARCS/Austria (Coray et al. 2002) in the city of Salzburg, reporting typical incident E-fields of 0.1-1 V/m in the proximity of cellular base stations. The expected peak spatial SAR in the brain for such incident E-field strengths is in the range of several μW/kg (Regel et al. 2006). An evaluation of European (German Federal Office for Radiation Protection 2005) mobile phone SAR data bases shows a mean peak spatial SAR_{10g} of mobile handsets operated at the human ear of 0.74 W/kg, measured according to CENELEC (2001). North American SAR data bases (Federal Communications Commission 2005) with measurements according to IEEE (2002) yield a mean SAR_{1g} of 0.96 W/kg. The induced fields are therefore several orders of magnitude higher for mobile handset exposure. These levels of daily exposure have triggered concern among health agencies and the public, since the highest exposed tissue is the central nervous system.

Recently, organ SAR values have been evaluated as a function of handsets (Kuster et al. 2004) based on generic phones or computer aided design (CAD) data of commercial

phones (Chavannes et al. 2003; Kainz et al. 2005). This preliminary study demonstrated a large dependence of the absorption on the handset design and its position with respect to the head for specific brain regions by a factor of greater than thirty (Chavannes et al. 2003). Various studies have addressed possible thermal effects by assessing the maximum temperature increases by mobile phone exposure. Although these studies lack a systematic worst-case approach, they demonstrate that the maximum temperature increase in the brain will not exceed 0.2-0.3°C for a peak spatial SAR of 2 W/kg averaged over 10 g of tissue (Hirata et al. 2003). These reported increases in temperature, however, do not exceed the general physiological fluctuations in temperature due to differences in metabolism and regional blood flow, time of day, extent of physical activity, ambient temperature, age, food supply or the menstrual cycle (Adair and Black 2003; Schmidt and Thews 2000). Consequently, the main effort is focused on possible non-thermal effects on the central nervous system, in particular the brain.

1.8 Base Station-Like Radio Frequency Electromagnetic Field Exposure

GSM and UMTS Exposure

To date, only few studies have been published with respect to the effects of base station exposure. In a survey study, Santini et al. (2003) collected symptoms related to “radiofrequency sickness” (Johnson Liakouris 1998) in people living in the vicinity of cellular phone base stations. In comparison with the reference group, complaints were experienced stronger by people located in the distance zones of < 10 m to 300 m from base stations. Whereas certain symptoms (e.g., nausea, loss of appetite) occurred in close vicinity of base stations only, other symptoms (e.g., irritability, sleep disturbances) were experienced only at a larger distance. Using a Spanish translation of a similar type of questionnaire, Navarro et al. (2003) reported a positive correlation between the subjects’ declared severity of symptoms and the measured GSM power densities in the corresponding bedrooms. A cross-sectional study by Hutter et al. (2006) revealed a significant relation of specific subjective symptoms (e.g., headache) and measured power densities in people living near mobile base stations, though in general the measured power levels were far below the guideline levels. Sleep quality, on the other hand, was more linked to the fear of adverse health effects than real EMF exposure. Perceptual speed in a reaction time task was increased, whereas no effect on accuracy

could be observed (Hutter et al. 2006). The so called “TNO study” (Zwamborn et al. 2003) explored both the effects of GSM and UMTS base station-like radiation on well-being and cognitive functions in 24 electrosensitive and 24 non-electrosensitive subjects. It was the first laboratory study to indicate a reduction in well-being in response to UMTS exposure in both groups of subjects, but there was no indication for an effect due to GSM electromagnetic fields. No consistent effect on cognitive performance in either study group was reported. In our follow-up study, however, the results were not confirmed (compare chapter 3.3). Likewise, a recent study by Hinrichs et al. (2005) failed to detect statistically significant effects on human sleep in response to far field GSM exposure. Thus, whereas observational studies may point to a relationship between near field base station-like exposure and reduced well-being, blinded provocation studies performed so far failed to confirm this observation. It should be noted that some papers mentioned here are methodologically questionable (e.g., no blinding of the study subjects: Navarro et al. 2003; Santini et al. 2003) and therefore should be critically reviewed with respect to the discussion about possible adverse health effects of base station electromagnetic field exposure.

1.9 Mobile Phone-Like Radio Frequency Electromagnetic Field Exposure

This chapter briefly summarizes the effects of RF EMF on electrophysiology and cognitive performance in humans reported in the literature so far. At this point, in addition, a short summary on electromagnetic hypersensitivity is provided. For a detailed overview of the published literature between 1995 and 2006, the interested reader is referred to chapter 2.

1.9.1 Effects on Electrophysiology

To present, most studies have used a handset-like signal to assess the effects of RF EMF exposure on brain physiology. One of the most commonly applied electro-physiological methods in humans to assess immediate changes in neural function is the EEG. In the last years, several studies investigated the influence of EMF emitted by cellular telephones on the spontaneous EEG of awake and sleeping subjects. Controversial observations were reported.

Most studies assessing the effects of RF EMF exposure in the awake state reported an increase in spectral power, particularly in the alpha frequency range during (e.g., Croft et

al. 2002; Curcio et al. 2005; D'Costa et al. 2003) or after exposure (Curcio et al. 2005; Hinrikus et al. 2004; Reiser et al. 1995; von Klitzing 1995). Whereas Reiser et al. (1995) reported a 15-min delayed increase in EEG power in the alpha2 (9.75-12.5 Hz), beta1 (12.75-18.5 Hz) and beta2 (18.75-35 Hz) frequency bands after mobile phone exposure, von Klitzing (1995) observed an immediate increase in alpha activity (~ 10 Hz) after having exposed the subjects for 15 min to an 150 MHz EMF applied via a special coil in the neck region. Hietanen et al. (2000) reported that an analogue Nordic Mobile Telephone (NMT) increased absolute centro-parietal delta power. In contrast, Röschke and Mann (1997) could not detect any significant differences between field-on and field-off conditions for any of the investigated frequency bands (delta, theta, alpha, beta).

Also with respect to the sleep EEG several effects of EMF exposure were observed. While some studies reported that exposure to EMF around 900 MHz affects conventional sleep parameters and spectral power mainly in the spindle frequency range (Borbély et al. 1999; Huber et al. 2000; 2002; Loughran et al. 2005; Mann and Röschke 1996; Pasche et al. 1996), not all studies were able to demonstrate such effects (e.g., Wagner et al. 1998; 2000). The observation of an increase in spectral power in the non-REM sleep EEG (7.25-14.25 Hz) during intermittent RF EMF exposure (Borbély et al. 1999) received further support by two studies of Huber et al. (2000; 2002) who reported increased spectral power in non-REM sleep in the 9-14 Hz frequency range after a 30-min exposure period. In addition to a shortened REM sleep latency, also Loughran et al. (2005) observed an increase of spectral power after handset-like exposure in stage 2 non-REM sleep, although in a slightly different frequency range (11.5-12.25 Hz). On the other hand, Wagner et al. (1998; 2000) failed to confirm the results of Mann and Röschke (1996) who reported decreased sleep onset latency, as well as a decreased duration and percentage of REM sleep after RF EMF exposure (900 MHz pulsed at 217 Hz) at a power flux density of 0.5 W/m^2.

In summary, a variety of effects were described in the last years. The reported effects mainly consisted of changes in the alpha frequency range in the wake EEG and in the spindle frequency range in stage 2 non-REM sleep. Recent studies demonstrated the crucial role of pulse modulation: only pulsed EMF exposure, but not continuous-wave EMF exposure increased EEG power in the alpha-frequency range (~ 10 Hz) in waking before sleep onset, as well as in the spindle-frequency range (12.25-13.5 Hz) in non-REM stage 2 sleep (Huber et al. 2002). Furthermore, it was suggested that the thalamus

as a subcortical structure with bilateral projections to the cortex might be more sensitive to RF EMF than other structures of the brain (Huber et al. 2002; 2003). This hypothesis was based on the fact that regardless of the side of exposure the effect on the sleep EEG was observed in both hemispheres. Because the thalamus received comparable exposure intensities in both experiments (~ 0.1 W/kg, Huber et al. 2002; 2003), the absence of hemispheric asymmetry can be explained. Since sleep spindles are generated in the thalamus (see chapter 1.4), an effect on the thalamus may explain the alterations in sleep spindle activity. Although this notion is consistent with the majority of published results, it is important to emphasize that EMF exposure was also found to affect other frequency bands, e.g., the delta band (Hietanen et al. 2000). In general, a comparison of the results is difficult as most studies varied with respect to factors such as exposure conditions and exposure duration, sample size, or the time point of EEG measurements.

In combined experiments of cognition and electrophysiology, probably the most common electrophysiological method used is the investigation of event related potentials (see chapter 1.2.2). In experiments examining the effects of RF EMF exposure on cognitive and sensory processing in humans, the tasks generally involve the measurement of reaction times, sensory discrimination, attention and working memory. Studies using ERPs to measure the effects of RF EMF exposure on brain activity have resulted in diverging results (e.g., Croft et al. 2002; Eulitz et al. 1998; Hinrichs and Heinze 2004; Jech et al. 2001; Krause et al. 2000b; Yuasa et al. 2006). For example, Krause et al. (2000a) reported altered ERD/ERS responses due to RF EMF exposure as a function of time in all frequency bands studied (4-6 Hz, 6-8 Hz, 8-10 Hz, 10-12 Hz) during retrieval, but not during encoding of an auditory memory task. Although this result was not replicated in a follow-up study (Krause et al. 2004), this finding is in line with a similar experiment of the same group (Krause et al. 2000b) where event related synchronization and desynchronization was altered due to RF EMF exposure during a verbal working memory task including three different memory workloads (0-, 1-, 2-back task). A study by Hamblin and colleagues (2004) revealed reduced N100 amplitude and latency to non-targets, but increased P300 latency to targets in an auditory oddball task. In two studies conducted by Freude and co-workers (1998; 2000), RF EMF exposure led to reduced slow brain potentials during a visual monitoring task, but not during simple self-paced

finger movements used to elicit a “Bereitschaftspotential” or a two stimulus task to elicit contingent negative variation.

In summary, although several studies reported an effect of short-term RF EMF exposure on ERPs, it is important to note that the reported results are difficult to compare. The usage of different cognitive tasks may have differently influenced ERP responses. Moreover, the findings of some studies are generally difficult to interpret because of a lack of information on several important experimental parameters (e.g., blinding conditions, dosimetry). The observed effects comprise a variety of components, amplitudes and latencies (e.g., N100, N200, P300, ESD/ESR) and were not always replicated under improved conditions (e.g., double-blind design, Krause et al. 2004).

1.9.2 Effects on Cognitive Performance

So far, different cognitive tasks with varying degrees of difficulty were used to measure effects of RF EMF exposure on cognitive performance (e.g., Besset et al. 2005; Croft et al. 2002; Freude et al. 2000; Krause et al. 2000a; 2000b; Preece et al. 1999). As currently no validated and reliable test or test battery exists, a variety of tasks has been implemented addressing different modalities, most of them measuring reaction times or accuracy of performance in response to moderate or higher cognitive workload (e.g., Edelstyn and Oldershaw 2002; Haarala et al. 2003b; Koivisto et al. 2000a; 2000b; Preece et al. 1999; Smythe and Costall 2003). Koivisto et al. (2000b) found shortened response times in simple reaction time and vigilance tasks after a 60-min EMF exposure period. In addition, the time needed to complete mental arithmetics was reduced and accuracy in the vigilance task was improved during the field-on compared to the field-off condition. Shortened reaction times were also reported in a second study of the same group for the high memory load portion of a sequential letter memory task (Koivisto et al. 2000a). Furthermore, Preece et al. (1999) reported faster reaction times in a two-choice reaction time task after analogue EMF exposure. In contrast, Freude et al. (2000) did not observe any effects on response times or accuracy scores due to exposure in different, but comparable tasks with respect to cognitive demands.

In summary, several studies reported either no effect, an increase or a decrease in speed or accuracy of performance in response to EMF exposure in a vast number of

cognitive tasks (e.g., Curcio et al. 2004; Edelstyn and Oldershaw 2002; Haarala et al. 2003b; Hamblin et al. 2004; Keetley et al. 2006; Koivisto et al. 2000a; Krause et al. 2000a; Lass et al. 2002; Preece et al. 1999). Yet, despite a growing amount of literature, results are inconsistent and outcomes of different tasks are difficult to compare. Moreover, some findings could not be replicated in recent follow-up studies (Haarala et al. 2003b; 2004; 2005; Krause et al. 2004; Preece et al. 2005), rendering conclusions even more difficult.

1.9.3 Electromagnetic Hypersensitivity

The extensive use of mobile phones as well as subjective health complaints attributed to EMF emission contributed to a public debate about possible adverse health effects of EMF exposure at intensities even below the general threshold in guidelines. The self-declared sensitivity to EMF is generally referred to as *electromagnetic hypersensitivity* (EHS). It includes non-specific symptoms and impaired well-being which are attributed to weak EMF (e.g., Ziskin 2002). The most frequent symptoms comprise dermatological symptoms (redness, tingling, and burning sensations) as well as neurasthenic and vegetative symptoms (fatigue, tiredness, concentration difficulties, dizziness, nausea, heart palpitation, and digestive disturbances). The collection of symptoms is not part of any recognized syndrome (World Health Organization 2005). The symptoms are mainly associated with exposure to power lines, mobile phones or mobile phone base stations, and also to a wide range of other electrical devices such as cordless telephones, visual display units or (domestic) power supply. Yet, despite a general reduction of well-being, experimental studies did not reveal a specific set of symptoms in response to mobile phone radiation (reviewed in Seitz et al. 2005). In the broadest sense, people who experience acute symptoms associated with few specific electrical devices can be distinguished from those who develop more severe symptoms in response to a wider range of electromagnetic stimuli (e.g., Bergdahl 1995). Because no validated tool (e.g., questionnaire) exists to reliably identify electrosensitive people, however, EHS corresponds to self-reported hypersensitivity and adequate medical treatment is difficult. A recent review by Rubin et al. (2006) indicates that compared to e.g., acupuncture, shielding procedures or supplementary antioxidant approaches, cognitive behavioral therapy may be most effective for people who consider themselves to be hypersensitive to weak radiation.

Independent of developing any symptoms, a majority of individuals with EHS frequently claims to sense EMF at very low intensities (Leitgeb and Schröttner 2003). In contrast, however, provocation studies suggest no correlation between the estimated RF condition and the real field condition in both subjects with and without EHS (reviewed in Seitz et al. 2005).

In summary, no conclusive evidence exists with respect to the existence of electromagnetic hypersensitivity. Controlled studies performed under double-blind conditions provide no indication that the symptoms correlate with RF EMF exposure or that EMF are detected more reliably by self-declared EHS subjects compared to the general public. Further laboratory studies are needed to either disprove EHS or identify and specify the exact conditions leading to the reported symptoms.

2 LITERATURE OVERVIEW

Human Studies on Radio Frequency Electromagnetic Field Exposure

This chapter provides a detailed overview on the literature that was summarized in chapter 1.9. It compares the effects of RF EMF exposure similar to mobile telephones on the awake and the sleep EEG, ERPs, regional cerebral blood flow (rCBF) and cognitive performance in humans and highlights some weaknesses of the respective studies. The main points on EMF parameters, sample size and blinding, measured variables and results of the respective studies are tabulated at the end of each paragraph. Possible reasons for the inconsistent findings are discussed in chapter 4.

2.1 Effects on the Waking Electroencephalogram

In the following, altogether eight studies published between 1995 and 2005 are summarized. The studies of Lebedeva et al. (2000) and Kramarenko and Tan (2003) are disregarded because of major deficiencies in the description of the methodology, the data analysis and the results.

Reiser et al. (1995) compared the effects of an electromagnetic field originating from a therapeutic instrument ("MEGA-WAVE 150/1", 150 MHz, modulated with 9.6 Hz) to a field originating from a digital mobile phone (902 MHz, modulated with 217 Hz). Three conditions ("MEGA-WAVE" exposure, mobile phone exposure, sham exposure) were applied at the same time of day with at least 24 h in between. In each condition, EEG recordings were started with a 15 min baseline recording. Experimental conditions were introduced in the second 15 min of recording in a randomized crossover design, always followed by 30 min without exposure. Precautions were taken to prevent influences of the EMF on the recording equipment. Subjects consisted of 18 males and 18 females. Statistical analysis revealed an increase in EEG power in the alpha2 (9.75-12.5 Hz), beta1 (12.75-18.5 Hz) and beta2 (18.75-35 Hz) frequency bands in both active field conditions. The increase due to the operation of the mobile phone, however, was seen with a delay of ~ 15 min after exposure. The experiment was performed under single-blind conditions. Artifacts were automatically eliminated and it remains open if the waking EEG was recorded with eyes closed or eyes open. Moreover, it is not specified on which side of the head the exposure conditions were applied (e.g., left/right side of

the head) and if “MEGA-WAVE” and mobile phone exposure exhibited the same maximal SAR.

von Klitzing (1995) observed an increase in alpha activity (~ 10 Hz) immediately after exposure of 17 subjects (male and female) for 15 min to an 150 MHz EMF applied via a special coil in the neck region. This increase was observed in the occipital lead (O2) under eyes closed conditions. The experiment was controlled for alterations in vigilance (subjects had to press a button within a time period of 20-30 s) and for influences of the EMF on the recording equipment. No information is given with respect to EOG and EMG recordings. Moreover, the dosimetry and the exposure conditions are not well described and the exact exposure duration is not specified (2 or 3 x 15 min). No information is provided with respect to the exact number of male and female subjects. The study was performed under single-blind conditions.

Röschke and Mann (1997) investigated the influence of a digital EMF (900 MHz pulsed at 217 Hz) on the waking EEG in 34 healthy male volunteers. Exposure was applied to the vertex of the head. Two consecutive ~ 10 min-EEG recordings (eyes closed) with a 30 min break in between were taken in the mornings (9:00-12:00 a.m.). Each recording was divided into three segments of 3.25 min each. Whereas the first and the third segment served as controls of vigilance, subjects were either exposed or sham exposed in the second segment in the first or the second EEG recording, respectively (randomized crossover design). Statistical analysis revealed no significant differences between field on and off conditions for any investigated frequency band (delta, theta, alpha, beta) or derivation (C3A1, C4A2). The experiment was performed under single-blind conditions. Information on EOG and EMG recordings are lacking and artifacts were eliminated automatically. It is not clear whether proper shielding of the amplifier was applied during the EEG recordings.

Hietanen et al. (2000) used five different mobile phones (three different 900 MHz analogue Nordic mobile telephones, one 900 MHZ digital GSM mobile phone, one 1800 MHz digital personal communication network phone (PCN)) to measure possible EMF effects on the awake brain. The EEG recording apparatus and the amplifier box were shielded against external interference. For 10 male and 9 female subjects, five 30-min waking EEG recordings (eyes closed) were taken consisting of 20 min RF EMF

exposure and 10 min sham exposure (5 min at the beginning and 5 min at the end of each recording). A sixths recording included a 30-min sham exposure only. The order of exposure conditions was randomized over subjects and recordings were performed on separate days. Exposure was applied to the left side of the head. The obtained results showed that only one of the analogue NMT mobile phones increased absolute centroparietal delta power. No effects were observed during exposure to the other four mobile telephones. The authors emphasized that this effect might have been observed by chance, as 180 t-tests were calculated in the process of statistical analysis. The study was performed single-blind. It is not clear whether all five exposure conditions exhibited the same maximal SAR. In general, the exposure conditions (e.g., side of exposure) and the dosimetry are not sufficiently described and information on EOG and EMG recordings are missing. No analysis of variance was applied prior to post-hoc testing.

Croft et al. (2002) measured EMF effects on waking EEG as well as on the early phase-locked neural response to auditory stimuli (this part of the study is summarized in chapter 2.3). Following a 3-min auditory discrimination task, waking EEG recordings (2 min) were performed with eyes open only to reduce possible alterations in vigilance. 24 subjects (16 males) repeated the 5-min EEG protocol for four times under three exposure conditions applied 5 cm radial to the subject's scalp midway between Oz and Pz (20 min EMF on, EMF off, attenuated EMF) in a single-blind counterbalanced crossover design. EMF exposure (EMF on) decreased delta activity (1-4 Hz) in the resting EEG and increased alpha activity (8-12 Hz) as a function of exposure duration. In general, the methodology and exposure conditions are insufficiently described (e.g., no information on shielding of the amplifier). The authors mention that the attenuated EMF condition is not specified as it is not relevant to the hypothesis being tested.

D'Costa et al. (2003) reported a slight decrease in mean EEG power during the full-power mode exposure to mobile phone EMF (central alpha (8-13 Hz), central and occipital beta (13-32 Hz)). In their pilot study, they recorded the waking EEG (eyes closed) in 5 male and 5 female subjects during emissions from a mobile phone positioned behind the head. In two distinct trials, the mobile phone was either emitting with "full power" or in "standby mode", respectively. In each trial, subjects were exposed to a randomized interrupted sequence of 5 x 5-min active and 5 x 5-min sham exposures (total recording duration: 50 min). Every 5-min EEG recording was followed by a

10 to 15-min break. In contrast to the “full-power” mode, no changes in EEG activity were observed in the standby mode trial. The subjects were not aware of the state of exposure (single-blind design). It is not clear whether EOG and EMG were recorded. Moreover, despite the long recording time with eyes closed, possible alterations in vigilance were not assessed. The shielding of the amplifier is not specified.

Hinrikus et al. (2004) studied the effects of photic stimulation and low level microwave radiation on human alpha and theta activity under eyes closed conditions. In the experiment, a baseline EEG recording (1 min) was followed by a 20-s photic stimulation. After a compensatory pause of 60 s, the 20 healthy subjects (11 males) were exposed on the left side of the head to 450 MHz microwave radiation modulated with 7 Hz. EMF exposure was repeated for 10 x 60 on-off-cycles. Continuous EEG recordings were performed during exposure as well as 60 s after stimulation. The amplifier was shielded against possible interferences due to the exposure. Compared to sham control, results demonstrated that photic stimulation caused a decrease in occipital alpha power in the majority of subjects, whereas EMF exposure basically increased frontal alpha power. The microwave induced changes became apparent with the third stimulation cycle. The authors stress, however, that due to the high interindividual variability no statistically significant observations in EEG activity levels could be observed for the whole group. The study was performed in a single-blind design. Information on EOG and EMG measurements are not provided though artifacts were detected by visual inspection. In general, the exposure conditions are not sufficiently specified.

In a recent study by Curcio et al. (2005), 20 healthy subjects (50% males) were randomly assigned to two experimental groups. While one group was exposed for 45 min to a 902.4 MHz EMF before a 7-min waking EEG recording, the wake EEG recording was antedated in the second group and occurred during the last 7 min of the 45-min of exposure. Exposure was applied on the left side of the head. In a double-blind randomized order, all subjects were submitted to 1) a baseline, 2) an active exposure, and 3) a sham exposure session, each separated by at least 48 h. At the central derivation (Cz), EMF exposure increased spectral power in the 9 Hz and 10 Hz bin when compared to baseline and sham control condition, respectively. A further increase due to EMF exposure was found at the parietal derivation (Pz) in the 11 Hz bin. Moreover, in

this lead the effect was stronger in the group of subjects exposed during the EEG recording. It is not clear whether the EEG recordings were performed under eyes closed or eyes open conditions. No information is provided with respect to the shielding of the amplifier, which is especially necessary as in one group of subjects recordings were taken during exposure.

Table 3: *RF EMF effects on the waking EEG (↑: significant increase; ↓: significant decrease; n.s.: no significant effect).*

Study	EMF Parameters [modulation in ()]	Sample size & Blinding	Measured variables	Results [compared to sham control]
(Reiser et al. 1995)	Exposure 1: "MEGA-WAVE", 150 MHz (9.6 Hz), 0.5 mW peak output power; 15-min exposure, behind the head, in 3-5 cm distance to skin	n=36 subjects (18 males) Single-blind	Waking EEG (EEG, EOG) (during + after exposure)	Exposure 1: ↑ Alpha2 (9.75-12.5 Hz), beta1 (12.75-18.5 Hz) and beta2 (18.75-35 Hz) power
	Exposure 2: Mobile phone, 902 MHz (217 Hz), 8 W peak output power; 15 min exposure, behind the head, in 40 cm distance to head, antenna centered			Exposure 2: ↑ Alpha2 (9.75-12.5 Hz), beta1 (12.75-18.5 Hz) and beta2 (18.75-35 Hz) power (with a delay of 15 min)
(von Klitzing 1995)	150 MHz (217 Hz), <1 mW/cm^2 power density; 2-3 x 15-min exposure; neck region, undefined distance	n=17 subjects (males & females) Single-blind	Waking EEG (EEG; eyes closed) (during + after exposure)	↑ Alpha (~10 Hz) immediately after exposure
(Röschke and Mann 1997)	900 MHz (217 Hz), 580 µs pulse width, 0.05 mW/cm^2 mean power density; 3.5-min exposure, vertex of head, antenna in 40 cm distance to vertex	n=34 subjects (males) Single-blind	Waking EEG (EEG; eyes closed) (during exposure)	n.s.

Study	EMF Parameters [modulation in ()]	Sample size & Blinding	Measured variables	Results [compared to sham control]
(Hietanen et al. 2000)	3 NMT analogue phones, 900 MHz 1 digital GSM phone, 900 MHz 1 digital PCN phone, 1800 MHz 1-2 W peak output power; 20-min exposure, left side of head, in 1±0.5 cm distance to head	n=19 subjects (10 males) Single-blind	Waking EEG (EEG; eyes closed) (during exposure)	↑ in absolute delta power (1 NMT mobile phone)
(Croft et al. 2002)	900 MHz (217 Hz), 577 µs pulse width, 3-4 mW estimated mean power (Nokia 5110); 20-min exposure, midway of head, in 5 cm distance to scalp	n=24 subjects (16 males) Single-blind	Waking EEG (EEG, EOG; eyes open) (during exposure)	↓ 1-4 Hz activity (right hemisphere) ↑ 8-12 Hz activity (midline posterior sides) as function of exposure duration
(D'Costa et al. 2003)	"Full-power": 900 MHz (217 Hz), 250 mW mean power (modified Nokia 6110); 25-min intermittent exposure, behind the head, antenna in 2 cm distance to head	n=10 subjects (5 males) Single-blind	Waking EEG (EEG; eyes closed) (during exposure)	↓ Central alpha (8-13 Hz) and beta (13-32 Hz) power ↓ Occipital beta power (13-32 Hz)
	"Standby modus": emitting low frequencies within 1-32 Hz[9] (Ericsson GH388); 25-min intermittent exposure, behind the head, antenna in 2 cm distance to head			n.s.

Study	EMF Parameters [modulation in ()]	Sample size & Blinding	Measured variables	Results [compared to sham control]
(Hinrikus et al. 2004)	Exposure 1: Photic stimulation, 20 s Exposure 2: 450 MHz (7 Hz), 50% duty cycle, 0.16 mW/cm^2 power density, SAR=0.0095 W/kg; ~10-min exposure, left side of head, in 10 cm distance to skin	n=20 subjects (11 males) Single-blind	Waking EEG (EEG, eyes closed) (during + after exposure)	Exposure 1: ↓ alpha power in all EEG channels (mainly occipital derivations) Exposure 2: ↑ alpha power in all EEG channels (mainly frontal derivations)
(Curcio et al. 2005)	902.4 MHz (217 Hz), 0.25 W mean power, SAR_{10g}=0.993 W/kg; ~45-min exposure, left side of head, in 1.5 cm distance to ear	n=20 subjects (10 males) Double-blind	Waking EEG (EEG, EOG, EMG) (during + after exposure)	↑ Alpha power (Cz: 9Hz,10 Hz bin) ↑ Alpha power (Pz: 11 Hz bin, especially during exposure)

2.2 Effects on Sleep and the Sleep Electroencephalogram

This chapter summarizes eight studies on the effects of RF EMF exposure on sleep architecture and EEG spectral power published between 1996 and 2005. As the study of Lebedeva et al. (2001) does not fulfill the general scientific criteria, it will not be included here.

Mann and Röschke (1996) reported a shortening of sleep onset latency as well as a suppression of REM sleep (amount, duration) and an increase in spectral alpha power (7.5-15 Hz) in REM sleep after 8-h nighttime exposure to a 217 Hz pulsed 900 MHz RF EMF. 12 male subjects (initially 14, 2 drop-outs) spent three 8-h nights (one adaptation night and two experimental nights) in the laboratory. A preliminary investigation excluded a direct influence of the electromagnetic field per se on the polysomnographic recording device. Conditions (field on vs. field off) were applied in a randomized crossover design at the vertex of the head. The reported hypnotic effect in this study was weak: sleep onset latency was only reduced ~ 3 min under RF EMF exposure. The shortening in REM sleep duration was not restricted to a specific part of the night and there was a trend to an increase in REM latency, leading to the authors' conclusion of a REM suppressing effect of the field. The study was presumably performed under single-blind conditions, however, it is not explicitly specified. Detailed information about the dosimetry is lacking. A subsequent double-blind study by Wagner et al. (1998) in 24 male subjects including a slightly lower mean power flux density than the one just mentioned (0.2 W/m^2 vs. 0.5 W/m^2) could not corroborate the effects. The contrasting findings were discussed as a possible dose-dependent effect or as being due to a difference in the absorbed radiation due to two different types of antennas used in the studies.

Due to the inconsistent results obtained, Wagner et al. (2000) reinvestigated the effects of RF EMF exposure (900 MHz pulsed at 217 Hz) on conventional sleep parameters and on sleep power spectra. Whereas the power flux density in the two previous studies was 0.5 W/m^2 and 0.2 W/m^2, respectively (Mann and Röschke 1996; Wagner et al. 1998), exposure resulted in an increased power flux density of 50 W/m^2 in this study. A simulation prior to the real experiment excluded a general influence of the EMF on EEG signaling. Each of the 20 male subjects spent two sessions of three consecutive nights in the sleep laboratory. The sessions were separated by a one-week

interval and consisted of either two nights of EMF exposure or sham control exposure, respectively. Thus 50% of the subjects were EMF exposed during the first session and 50% during the second session. Exposure was applied below the pillow of the bed and took place in a shielded chamber during the whole 8-h sleep period. In accordance to Wagner et al. (1998), statistical comparison of exposure conditions revealed no significant effect on conventional sleep parameters or on sleep EEG power spectra (total power as well as defined frequency bands). The study was performed under single-blind conditions.

Pasche et al. (1996) used low energy emission therapy (LEET) to study the effect on chronic psychophysiological insomnia in 106 (47 males) patients. The study was conducted in two different centers in a double-blind design. The treatment comprised 20-min LEET exposure prior to sleep via a mouthpiece three times per week between 3:00-8:00 p.m. for altogether four weeks. All subjects stayed at least 6 h, but not more than 8.5 h in bed. Volunteers with psychophysiological insomnia were subdivided into an active or an inactive treatment group in a randomized design. Comparing the polysomnographical recordings of the baseline night and the last treatment night (n = 97, 8 dropouts) revealed a decrease in sleep latency, an increase in total sleep time and sleep efficiency, as well as an increased number of sleep cycles without altering the percentage of the various sleep stages during the night. No effects on waking after sleep onset were reported. A significant increase in non-REM sleep in the active group is mentioned in the results section, but not in the abstract. The exposure conditions are not sufficiently described. No information is provided regarding the gender or age of the dropouts. The demographic description of the study population includes all 106 subjects.

During an 8-h nighttime sleep episode, Borbély et al. (1999) exposed 24 healthy young males to an intermittent electromagnetic field (cycles of 15 min on- and off-intervals) and compared it to a night of sham exposure. The two exposure conditions (EMF, sham) were applied in a double-blind randomized crossover design consisting of two sessions separated by a one-week interval. Each session comprised one adaptation night and one experimental night, respectively. Beds were surrounded by absorber walls and the antennas were fixed in 30 cm distance behind the subjects head. Electromagnetic interferences were prevented by appropriate shielding of the recording system. Compared to the sham control condition, the 900 MHz RF EMF statistically

reduced waking after sleep onset. Moreover, spectral activity in non-REM sleep (7.25-14.25 Hz) was increased mainly in the beginning of the night with peaks at 10-11 Hz and 13.5-14 Hz frequency bands. The increased spectral power in the non-REM sleep EEG during intermittent RF EMF exposure received further support by a study of Huber et al. (2000). In a double-blind design, 16 healthy male subjects were unilaterally exposed for 30 min to a RF EMF prior to a 3-h morning sleep episode. Preceding night-time sleep was restricted to 4 h to enhance sleep propensity. Altogether three sessions (left side EMF exposure, right side EMF exposure, sham exposure) were applied, each separated by a one-week interval. EMF (900 MHz) or sham exposure occurred in a randomized double-blind crossover design. Whereas no effects on sleep parameters were observed, spectral power in non-REM sleep was increased in the 9-14 Hz frequency range (9.75-11.25 Hz; 12.25-13.25 Hz). This effect was independent of the side of exposure (left or right side of head) and decreased in the course of the night. Additional analyses and a detailed dosimetry for the studies performed by Borbély et al. (1999) and Huber et al. (2000) were published by Huber et al. (2003).

In a further study, Huber et al. (2002) investigated the effects of an unilateral 30-min EMF exposure prior to sleep on the waking and an 8 h-sleep EEG in 16 healthy male volunteers. Besides the pulse-modulated RF EMF, an additional 900 MHz continuous-wave (CW) EMF was applied. The experiments were carried out in a double-blind crossover design. Pulsed EMF exposure resulted in an increase in EEG power in the alpha-frequency range (~ 10 Hz) in waking before sleep onset as well as in the spindle-frequency range (12.25-13.5 Hz) of the EEG in non-REM stage 2 sleep. The enhancement of power in the sleep spindle frequency range paralleled the general increasing trend of spindle frequency activity and was largest in the fourth and fifth non-REM sleep episodes. No effects of CW EMF exposure could be observed. The authors therefore concluded that pulse modulation of EMF might be necessary to induce observable effects in the waking and the sleep EEG. The study design was not fully balanced.

Loughran et al. (2005) reported an increase in spectral EEG power in the spindle frequency range (11.5-12.25 Hz) of stage 2 non-REM sleep after 30-min exposure to a digital mobile phone handset compared to sham control. This change was observed in the first non-REM sleep episode. In addition, REM sleep latency was decreased by

~ 17 min. Exposure or sham exposure was applied ~ 20 min prior to a 7.5-h sleep episode in 27 male and 23 female subjects at the right side of the head. The exposure conditions were applied in a double-blind design in two experimental sessions one week apart, including one adaptation and one exposure night, respectively.

Table 4: *RF EMF effects on sleep and the sleep EEG (↑: significant increase; ↓: significant decrease; n.s.: no significant effect).*

Study	EMF Parameters [modulation in ()]	Sample size & Blinding	Measured variables	Results [compared to sham control]
(Mann and Röschke 1996)	900 MHz (217 Hz), 580 µs pulse width, 0.05 W/m^2 mean power density (Motorola phone); 8-h exposure, vertex of head, in 40 cm distance to vertex	n=14 subjects (males) Single-blind (+ blind scoring)	Sleep EEG (8h; EEG, EOG, EMG, ECG) (during exposure)	↓ Sleep onset latency ↓ Duration and percentage of REM sleep ↑ Alpha power (7.5-15 Hz) during REM sleep
(Pasche et al. 1996)	LEET (27.12 MHz, modulation band width 0.1 Hz-10 kHz), SAR <2 W/kg; 20-min exposure (3 x per weeks, altogether 12 times), mouthpiece	n=106 subjects (47 males) Double-blind	Sleep EEG (6-8.5h; EEG, EOG, EMG, ECG) (after exposure)	↓ Sleep latency ↑ Total sleep time ↑ Sleep cycles (without altering percentage of sleep stages during night)
(Wagner et al. 1998)	900 MHz (217 Hz), 577 µs pulse width, 0.2 W/m^2 mean power density, SAR=0.3 W/kg (vertex), SAR_{peak}=0.6 W/kg neck) (Motorola phone); 8-h exposure, antenna below the pillow, in 40 cm distance to pillow	n=24 subjects (males) Single-blind (+ blind scoring)	Sleep EEG (8h; EEG, EOG, EMG, ECG) (during exposure)	n.s.
(Borbély et al. 1999)	900 MHz base station-like signal (2, 8, 217, 1736 Hz and higher harmonics), 87.5% duty cycle, SAR_{10g}=1 W/kg; 8-h intermittent exposure (15 min on / off), behind the head, antennas in 30 cm distance to head	n=24 subjects (males) Double-blind	Sleep EEG (8h; EEG, EOG, EMG, ECG) (during exposure)	↓ Waking after sleep onset ↑ Spectral power in non-REM sleep EEG (10-11 Hz; 13.5-14 Hz)

Study	EMF Parameters [modulation in ()]	Sample size & Blinding	Measured variables	Results [compared to sham control]
(Huber et al. 2000)	900 MHz base station-like signal (2, 8, 217, 1736 Hz), 87.5% duty cycle, SAR_{10g}=1 W/kg; 30-min exposure; left/right side of head, patch antenna in 11 cm distance to ear	n=16 subjects (males) Double-blind	Sleep EEG (8h; EEG, EOG, EMG, ECG) (after exposure)	↑ Spectral power in non-REM sleep EEG (9.75-11.25 Hz; 12.25-13.25 Hz)
(Wagner et al. 2000)	900 MHz (217 Hz), 577 µs pulse width, 50 W/m^2 mean power density, SAR_{10g}<2 W/kg (Motorola 1000); 2 x 8-h exposure, antenna below the pillow, in 40 cm distance to pillow	n=20 subjects (males) Single-blind	Sleep EEG (2 nights à 8h, EEG, EOG, EMG, ECG) (during exposure)	n.s.
(Huber et al. 2002)	900 MHz handset-like signal (2, 8, 217, 1736 Hz), 12.5% duty cycle 900 MHz continuous-wave SAR_{10g}=1 W/kg; 30-min exposure, left side of head, antenna in 11 cm distance to ear	n=16 subjects (males) Double-blind	Sleep EEG (8h; EEG, EOG, EMG, ECG) (after exposure)	↑ Alpha power (~10 Hz) in waking EEG before sleep onset ↑ Non-REM EEG spectral power (12.25-13.5 Hz)
(Loughran et al. 2005)	894.6 MHz (217 Hz), 12.5 % duty cycle, 0.25 W mean power, SAR_{10g}=0.11 W/kg, SAR_{peak}=0.29 W/kg (modified Nokia 6110); 30-min exposure, right side of head, phone oriented in normal position of use	n=50 subjects (27 males) Double-blind	Sleep EEG (7.5h, EEG, EOG, EMG, ECG) (after exposure)	↓ REM sleep latency ↑ EEG non-REM sleep power density in 11.5-12.25 Hz frequency range

2.3 Effects on Event Related Potentials

Various studies examined the effects of EMF exposure on human brain oscillatory activity during cognitive processing (compare chapter 1.2.2). 11 studies between 1998 and 2006 are summarized in this chapter. The studies of Papageorgiou et al. (2004) and Urban et al. (1998) do not fulfill basic scientific requirements and are therefore excluded.

Eulitz et al. (1998) used an oddball paradigm to investigate the brain response to a 916.2 MHz RF EMF pulsed at 217 Hz. A mobile phone was mounted to the left side of the subjects head (13 males) while performing an auditory discrimination task with four blocks of 450 stimuli each (two blocks with “field on”). Compared to sham control, statistical analysis of EEG spectral data in the time window of P300 occurrence (260-380 ms) revealed that RF EMF exposure modulated the induced (frequency-domain analysis), but not the evoked brain response (averaged EEG responses), however, to task relevant stimuli only. This effect was observed in higher frequency bands (18.75-31.25 Hz) and mainly in the exposed hemisphere (left posterior temporal region). The study was performed under single-blind conditions. The exact exposure duration as well as the time interval between sham and real exposure is not specified. No information is provided with respect to the shielding of the amplifier. The dosimetry is not sufficiently described.

In a single-blind crossover design, Freude et al. (1998) examined preparatory slow brain potentials in a low demanding (simple self-paced finger movements) and a high demanding (visual monitoring, VMT) task. 16 healthy right-handed male subjects performed both tasks (~ 8 min) in succession during either 916.2 MHz EMF exposure or sham exposure. Exposure conditions were counterbalanced between subjects and applied to the left side of the head. EMF exposure led to a reduction in slow brain potential amplitude in the VMT. These differences were more pronounced over the right than over the left hemisphere. The time interval between sham and exposure condition is not specified. The same group performed a similar study investigating the influence of EMF exposure on left side of the head on brain activity in two separate experiments about 6 months apart from each other (Freude et al. 2000). In both experimental setups, healthy right-handed male subjects (n = 20 and 19, respectively) performed a complex and demanding visual monitoring task (VMT, compare Freude et al. 1998). In experiment 1, tasks were performed in blocks of 30 trials (~ 3 min), in experiment 2 in

blocks of 50 trials (~ 4 min). In experiment 2, two additional tasks were included: a *"Simple finger movement task"* and a *"Two-stimulus task"* to elicit a "Bereitschafts-potential" (BP) and a contingent negative variation (CNV), respectively. Performance parameters comprised accuracy (VMT), the time interval of self-paced key presses (BP) and reaction times (CNV). Due to an excessive number of artifacts, only 16 subjects were included in the analysis of the first experiment. In line with previous findings, (Freude et al. 1998) a significant decrease of slow brain potentials in the high demanding visual monitoring task was found during EMF exposure in both experiments. This effect was seen in all derivations except the frontal ones, mainly over the right hemisphere. In contrast, results in the simple finger movement task and the two-stimulus task were not significantly altered during EMF exposure. No effect on performance was found. The study was performed under single-blind conditions. The exposure conditions are not well specified and the exact exposure duration is not mentioned. No information is provided with respect to the shielding of the amplifier.

Krause et al. (2000a) successively exposed 16 healthy right-handed volunteers (8 males and 8 females) for 30 min to either an 902 MHz EMF pulsed at 217 Hz or to a sham control condition in a counterbalanced crossover design (single-blind). During exposure of the right side of the head, subjects performed an auditory memory task (modified Sternberg memory search paradigm) while EEG and EOG were recorded. Analysis of ERS and ERD (compare chapter 1.2.2) of 4-6 Hz, 6-8 Hz, 8-10 Hz, 10-12 Hz EEG frequency bands revealed a significant increase in relative power in the lower alpha range (8-10 Hz) during EMF exposure. In addition, EMF exposure altered the response as a function of time in all studied frequency bands during retrieval, but not during encoding of the four-verb memory set. Although the results could not be replicated in a follow-up study under double-blind conditions with a larger sample size (12 male, 12 female subjects, Krause et al. 2004), this finding is in line with a similar experiment of the same group under comparable exposure conditions (Krause et al. 2000b) where RF EMF effects on ERD/ERS were examined by means of a working memory task including three different memory workloads (N-back task; 0-, 1-, 2-back; see also the Appendix). 24 healthy subjects (12 males) were investigated. Whereas no EMF effects on reaction time or accuracy of performance were found, EMF exposure decreased the difference between the ERD/ERS responses elicited by targets and non-targets. This effect was most prominent in the left hemisphere. In the 6-8 Hz frequency band the presence of the

EMF led to an enhancement as well as a delay in the ERD responses in the 0- and 1-back task specifically after the presentation of target stimuli. In contrast, in the 2-back task, the EMF enhanced the early ERS (100-300 ms) after the presentation of non-targets. Both studies were performed single-blind. Due to computational problems only 14 subjects were included in the final analysis in Krause et al. (2000a) and a varying number of subjects (n = 16-21) in Krause et al. (2000b). Sequence effects should be taken into account as the design was no longer counter-balanced. Moreover, no break was applied between the exposure and non-exposure in the first study (Krause et al. 2000a) and only a 5-min break in the second study (Krause et al. 2000b), so that carry-over effects between the exposure conditions cannot be excluded.

Jech et al. (2001) exposed or sham exposed 9 male and 13 female patients with narcolepsy-cataplexy for 45 min and investigated a possible effect on brain activity and reaction times. A subgroup of 17 subjects performed a visual oddball task on two successive days, with the task starting after 5 min of exposure of the right side of the head to a 900 MHz mobile phone continuously transmitting at 2 W maximum power. Prior to examinations, each patient was allowed to sleep for 20 min. After 45 min of exposure, the RF EMF was turned off and EEG recordings were started after further 15 min while the patient was allowed to fall asleep. Whereas no effects on latencies were found, EMF exposure resulted in a decreased N200 amplitude, an increased P300 amplitude and shortened reaction times to the target stimuli. No alterations due to EMF exposure were found in spontaneous EEG recordings. The study was performed in a double-blind design. Prior to exposure and during EEG recordings, subjects were allowed to nap for max. 20 min. It is not mentioned how many patients did nap and for how long or if the amplifiers were shielded during EEG recordings. Therefore, the reported results are difficult to evaluate. The description of the data analysis is generally insufficient.

Croft et al. (2002) measured EMF effects on the early phase-locked neural response to auditory stimuli. Reaction time and accuracy of performance were collected within the auditory discrimination task. After completion of the task (3 min), the resting EEG was recorded for 2 min (this part of the study is summarized in chapter 2.1). 24 subjects (16 males) repeated the 5-min EEG protocol for four times under three exposure conditions applied 5 cm radial to the subject's scalp midway between Oz and

Pz (20 min EMF on, EMF off, attenuated EMF) in a counterbalanced crossover design. The phase-locked neural response in the discrimination task revealed an attenuation of the normal power decrement over time in the theta band, a general reduction in beta power as well as an increase in gamma power during EMF on conditions. The study was performed single-blind. In general, the methodology and exposure conditions are insufficiently described (e.g., no information on shielding of the amplifier). The authors mention that the attenuated EMF condition is not specified as it is not relevant to the hypothesis being tested.

In a study by Hamblin and colleagues (2004), 12 healthy subjects (4 males) attended two sessions one week apart and underwent EMF or sham exposure in a counterbalanced crossover design. Exposure lasted 60 min. During the first half of exposure (30 min) subjects performed practice trials of an auditory oddball task. These were followed by test trials in the second half of exposure. Exposure was applied to the right side of the head and increased response times but had no effect on accuracy. Moreover, it reduced the N100 amplitude and latency to non-targets over the midline and right hemisphere sites but increased P300 latency to targets at left frontal and left central sites. The study was performed single-blind.

Twelve healthy volunteers (2 males) in the study of Hinrichs and Heinze (2004) performed an encoding task, in which a list of items had to be memorized. Subjects were exposed for 30 min to an active or an inactive mobile phone (left side of the head) in a double-blind counterbalanced design. During the last 10 min of exposure, a list of 200 words was presented. During the retrieval phase 15 min later, subjects had to discriminate the familiar words from new words in a 500-item test list. Moreover, magnetoencephalographic recordings were taken in order to gain spatial-temporal information. EMF exposure did not affect behavioral data (reaction time, accuracy of performance) but changed an early (350-400 ms) task-specific component of the evoked related MEG. The authors concluded that this points to an interference of the EMF and item encoding.

Just recently, Yuasa and coworkers (2006) published data on the effect of a 30-min EMF exposure on somatosensory evoked potentials (SEP) in order to evaluate the influence of short term RF EMF exposure on sensory cortex functioning. Single pulse

SEPs as well as a paired stimulation technique to assess the effect on recovery function were applied in 12 subjects (5 males) and an unspecified subgroup of altogether seven subjects, respectively. The recordings were performed prior to and directly after a real or a sham exposure. During the two exposure conditions, the subject had to hold a mobile phone in normal position to their right ear. SEPs were recorded from the hand sensory area of the right hemisphere after left median nerve stimulation. Statistical analysis did not reveal any significant effects on single SEPs or their recovery function. As the subjects had to hold the mobile phone to the ear during the 30-min exposure, no standardized exposure conditions were provided. Information on a single- or double-blind design is missing. Moreover, for the subgroup the number of male and female subjects is not specified.

Table 5: *RF EMF effects on ERPs (↑: significant increase; ↓: significant decrease; n.s.: no significant effect).*

Study	EMF Parameters [modulation in ()]	Sample size & Blinding	Measured variables	Results [compared to sham control]
(Eulitz et al. 1998)	916.2 MHz (217 Hz), 577 µs pulse width, 2.8 W peak power; undefined exposure duration, left side of head, undefined distance	n=13 subjects (males) Single-blind	ERPs (EEG)	
			Auditory discrimination task	↑ P300 (mainly left hemisphere)
			(during exposure)	
(Freude et al. 1998)	916.2 MHz (217 Hz), 577 µs pulse width, 2.8 W peak power, SAR_{1g}=1.42 W/kg, SAR_{10g}=0.882 W/kg; 8-min exposure, left side of head, in direct contact to ear	n=16 subjects (males) Single-blind	ERPs (EEG, EOG)	
			Simple self-paced finger movements	n.s.
			Visual monitoring task	↓ of slow brain potentials (central, temporo-parieto-occipital brain regions; mainly right hemisphere)
			(during exposure)	
(Freude et al. 2000)	916.2 MHz (217 Hz), 577 µs pulse width, 2.8 W peak power, SAR_{1g}=1.42 W/kg, SAR_{10g}=0.882 W/kg;		ERPs (EEG, EOG)	
	Experiment 1: undefined exposure duration, left side of head, in direct contact to ear	Experiment 1: n=20 subjects (males) Single-blind	Experiment 1: Visual monitoring task	Experiment 1: ↓ of slow brain potentials (central, temporo-parieto-occipital brain regions; mainly right hemisph.)
			(during exposure)	
	Experiment 2: undefined exposure duration, left side of head, in direct contact to ear	Experiment 2: n=19 subjects (males) Single-blind	Experiment 2: Visual monitoring task	Experiment 2: ↓ of slow brain potentials (central, temporo-parieto-occipital brain regions; mainly right hemisph.)
			Simple self-paced finger movements	n.s.
			Two-stimulus task	n.s.
			(during exposure)	n.s. (cognitive performance)

Study	EMF Parameters [modulation in ()]	Sample size & Blinding	Measured variables	Results [compared to sham control]
(Krause et al. 2000a)	902 MHz (217 Hz), 577 µs pulse width, 0.25 W mean net forward power; 30-min exposure, right side of head, antenna in ~20 mm distance to skin	n=16 subjects (8 males) Single-blind	ERPs (EEG, EOG) Auditory memory task (during exposure)	↑ relative power (8-10 Hz) Altered responses in all frequency bands as a function of time during retrieval only: 4-6 Hz: decreased and delayed ESR response (~200-800 ms) 6-8 Hz: enhanced ERS (~200-600 ms) and decreased ERD responses (~600-1500 ms) 8-10 Hz: enhanced ERD/ERS responses (~100- 700 ms) 10-12 Hz: enhanced ESR response (~200-500 ms)
(Krause et al. 2000b)	902 MHz (217 Hz), 577 µs pulse width, 0.25 W mean net forward power, SAR <2 W/kg; 30-min exposure, right side of head, antenna in ~20 mm distance to skin	n=24 subjects (12 males) Single-blind	ERPs (EEG, EOG) N-back task (0-, 1-, 2-back) (during exposure)	↓ relative power (4-6 Hz) after presentation of targets in the 0-, 1-back task ↑ relative power (8-10 Hz) after presentation of non-targets in 2-back task n.s. (cognitive performance)
(Jech et al. 2001)	900 MHz (217 Hz), 577 µs pulse width, 2 W max. power output, SAR_{10g}=0.06 W/kg (Motorola d520); 45-min exposure, right side of head, fixed to the ear	n=22 narcoleptic patients (9 males) Double-blind	ERPs (EEG, EOG) Visual oddball task (during exposure)	↓ N200 amplitude ↑ P300 amplitude ↓ Reaction times to targets

Study	EMF Parameters [modulation in ()]	Sample size & Blinding	Measured variables	Results [compared to sham control]
(Croft et al. 2002)	900 MHz (217 Hz), 577 µs pulse width, 3-4 mW estimated mean power (Nokia 5110); 20-min exposure, midway of head, in 5 cm distance to scalp	n=24 subjects (16 males) Single-blind	ERPs (EEG, EOG) Auditory discrimination task (during exposure)	↓ 4-8 Hz band power as function over time ↓ 12-30 Hz band power globally and as function over time ↑ 30-45 Hz band power (midline frontal and lateral posterior sides)
(Hamblin et al. 2004)	894.6 MHz (217 Hz), 576 µs pulse width, 2 W peak power, SAR=0.87 W/kg (modified Nokia 6110); 60-min exposure, right side of head, phone oriented in normal position of use	n=12 subjects (4 males) Single-blind	ERPs (EEG) Auditory oddball task (during exposure)	↓ N100 amplitude + latency to non-targets (larger right midline) ↑ P300 latency to targets (larger left frontal + central derivations) ↑ Reaction times
(Hinrichs and Heinze 2004)	1870 MHz (217 Hz), 0.125 W average power (1 W peak power), SAR_{1g}=1.14 W/kg SAR_{10g}=0.61 W/kg; 30-min exposure, left side of head, close to ear	n=12 subjects (2 males) Double-blind	(MEG; EOG) Word list (during exposure, last 10 min)	Change in early (350-400 ms) task-specific component of the event related MEG (left occipito-parietal sensors) n.s. (cognitive performance)

Study	EMF Parameters [modulation in ()]	Sample size & Blinding	Measured variables	Results [compared to sham control]
(Krause et al. 2004)	902 MHz (217 Hz), 577 µs pulse width, 0.25 W mean net forward power, SAR_{10g}=0.648 mW/kg (SAR_{1g}=0.878 mW/kg); 30 min exposure, left side of head, 40 mm distance	n=24 subjects (12 males) Double-blind	ERPs (EEG, EOG) Auditory memory task (during exposure)	 4-6 Hz: decreased ERS response 6-8 Hz: decreased ERS during memory retrieval over left hemisphere ↑ Mean percentage of incorrect answers
(Yuasa et al. 2006)	800 MHz (50 Hz) 270 mW average power; SAR_{10g}=0.054 ±0.02 mW/kg; 30 min exposure, right side of the head, phone with hand to head (antenna in ~4 cm distance)	n=12 subjects (5 males) No blinding	ERPs (EEG) Somatosensory evoked potentials (before + after exposure)	 n.s.

2.4 Effects on Regional Cerebral Blood Flow

All three studies published on RF EMF induced changes on rCBF between 2002 and 2006 are reviewed. A very recent paper on brain excitability via transcranial magnetic stimulation (TMS) is summarized at the end of this section.

In a positron emission tomography (PET) study, Huber et al. (2002; 2005) investigated the effects of an unilateral 30-min EMF exposure on rCBF in 16 healthy male volunteers. Exposure was applied prior to three measurements (~ 10 min, 20 min and 30 min after exposure). RF EMF exposure comprised a base station-like signal (compare Borbély et al. 1999), as well as a handset-like signal (compare Huber et al. 2000) and a sham control condition. The experiment was carried out in a randomized double-blind crossover design. Intervals between exposure conditions were at least one week. Compared to sham control, the pulsed EMF exposure increased the regional cerebral blood flow in the dorsolateral prefrontal cortex ipsilateral to the side of exposure (left side exposure, Huber et al. 2002). In a further analysis and in line with this finding, Huber et al. (2005) observed increased rCBF in the dorsolateral prefrontal cortex on the side of exposure after handset-like exposure, but not after base station-like exposure. Due to technical problems only the data of 13 subjects (Huber et al. 2002) and 12 subjects (Huber et al. 2005) were introduced to statistical analysis. In general, regions exhibiting high-level exposure were larger than those showing significant changes in rCBF. Therefore, the changes in rCBF after exposure did not correspond with the simulated distribution of the SAR. Due to three and four dropouts, respectively, the order of exposure conditions was not balanced.

In a double-blind study by Haarala et al. (2003a) 14 male volunteers served as a study sample to investigate the influence of ~ 45-min GSM exposure on rCBF and working memory. Exposure and PET scans were performed simultaneously and conditions (EMF vs. sham) were counterbalanced over subjects. Exposure was applied to the left side of the head. The memory task (N-back task) was performed under both conditions so that every subject served as his own control. The 902 MHz EMF exposure produced a relative decrease in rCBF in the auditory cortex of both hemispheres (Brodmann area 41). As the active mobile phone condition induced a subliminal audible noise, however, the authors themselves concluded that the bilateral change in blood flow might not be due to EMF exposure itself but simply to acoustic signals produced by the

mobile phone. Indeed, if the mobile phone was not battery operated, no effect in the auditory cortex was observed. No effects on reaction time or accuracy of performance were observed in the N-back task. As only 12 subjects were included in the analysis (10 subjects with respect to the cognitive tasks), sequence effects should be included in the analysis as a balanced design is questionable. Both exposure conditions were applied consecutively so that carryover effects cannot be excluded.

Without a specified a priori hypothesis with respect to the location of effects, Aalto et al. (2006) studied the effects of a 902 MHz RF EMF on rCBF using 1.5 Tesla PET imaging. EMF or sham exposure lasted for 51 min, respectively, and were applied to the left side of the head during PET data acquisition in a double-blind counterbalanced order (15 min between conditions). During PET scans, the 12 healthy male subjects repetitively performed a 1-back task with the same sequence of letters. While no effect on cognitive performance was observed, EMF exposure decreased rCBF beneath the antenna in the posterior inferior temporal cortex (left fusiform gyrus). In contrast, EMF exposure increased rCBF bilaterally in the superior and medial frontal gyri. As in the study of Haraala et al. (2003a), both exposure conditions were applied consecutively with only 15 min in between, so that carryover effects cannot be excluded. No parallel test forms of the 1-back task were applied. Moreover, in all conditions the same sequence of letters was used so that learning effects cannot be excluded.

Ferreri et al. (2006) tested the excitability of the left and the right brain hemisphere after real or sham exposure by means of paired pulse TMS (pp TMS). 15 healthy male subjects were exposed in two sessions one week apart to a 902.4 MHz EMF or a sham control condition in a double-blind crossover design. Exposure duration was 45 min. Motor-evoked potentials of the two hemispheres were recorded during TMS over the primary motor cortex using a paired pulse paradigm prior to as well as immediately after exposure. An additional recording was performed after a 1-h rest interval. Recordings were always started on the left hemisphere and tympanic temperature of both ears was measured before each TMS recording. Whereas no effect on resting motor threshold and single pulse TMS was observed, an excitability change due to real EMF vs. sham exposure occurred in the left hemisphere. Specifically, short intracortical inhibition was reduced, whereas facilitation was enhanced in the acutely exposed left hemisphere compared with the non-exposed right hemisphere or sham exposure. Recordings post

exposure revealed that these effects vanished after a break of 1 h. Tympanic temperature was not affected in either condition.

Table 6: *RF EMF effects on rCBF (↑: significant increase; ↓: significant decrease; n.s.: no significant effect).*

Study	EMF Parameters [modulation in ()]	Sample size & Blinding	Measured variables	Results [compared to sham control]
(Huber et al. 2002; 2005)	Exposure 1: 900 MHz (2, 8, 217, 1736 Hz), 12.5% duty cycle, SAR_{10g}=1 W/kg; 30-min exposure, left side of head, patch antenna in 11 cm distance to ear	n=16 subjects (males) Double-blind	rCBF (after exposure)	Exposure 1: ↑ rCBF (left dorsolateral prefrontal cortex)
	Exposure 2: 900 MHz base station signal (2, 8, 217, 1736 Hz), 87.5% duty cycle, SAR_{10g}=1 W/kg; 30-min exposure, left side of head, patch antenna in 11 cm distance to ear			Exposure 2: n.s.
(Haarala et al. 2003a)	902 MHz (217 Hz), 577 µs pulse width, 0.25 W mean power, SAR_{max}=0.5 W/kg (Motorola Timeport 260); ~45-min exposure, left side of head, antenna in ~17 mm distance from surface of the skull	n=14 subjects (males) Double-blind	rCBF N-back (0-, 1-, 2, 3-back) (during exposure)	↓ rCBF (bilateral auditory cortex) n.s.
(Aalto et al. 2006)	902 MHz (217 Hz), 577 µs pulse width, 0.25 W mean power, SAR_{10g}=0.743 W/kg; 51-min exposure, left side of head, antenna in ~17 mm distance from surface of the skull	n=12 subjects (males) Double-blind	rCBF (during exposure) N-back (1-back)	↓ rCBF (left fusiform gyrus, posterior inferior temporal cortex) ↑ rCBF (bilateral, superior and medial frontal gyri) n.s.

Study	EMF Parameters [modulation in ()]	Sample size & Blinding	Measured variables	Results [compared to sham control]
(Ferreri et al. 2006)	902.4 MHz (217 Hz), 0.25 W mean power, SAR=0.05 W/kg; 45-min exposure, left side of head, in 15 mm distance to ear	n=15 subjects (males) Double-blind	Brain excitability (pp TMS) (before + after exposure)	↑ Brain excitability (intracortical inhibition reduced, facilitation enhanced)

2.5 Effects on Cognitive Performance

Several studies have been published with respect to the effects on reaction times and accuracy of performance in various cognitive tasks. This overview includes 17 studies between 1999 and 2006. The study of Lee et al. (2001) will not be summarized in this overview as the study sample was not actively exposed to a mobile phone condition but chosen on the basis of being a mobile phone user. The study of Hladký et al. (1999) does not fulfill basic scientific criteria and is therefore excluded.

Preece et al. (1999) studied the effects of a 915 MHz RF EMF on performance in a series of cognitive tests. Besides a digital pulsed field (217 Hz) and a sham control condition, an analogue field was applied in 36 healthy volunteers in two study groups (50% males) in a randomized crossover design. The left side of the head was exposed for 25-30 min. The three exposure sessions were conducted with a 48-h break in between. Parallel test forms of the cognitive tasks were presented. The results showed that response times in the two-choice reaction time task were speeded up during analogue EMF exposure, but not during pulsed RF EMF exposure. This finding was strengthened by the fact that the consideration of confounding factors (e.g., sleep, consumption of alcohol or caffeine) did not alter the result. It is important to stress, however, that the two applied field conditions are difficult to compare as the mean net forward output power of the phones differed tremendously (analogue field: 1 W; pulsed field: 0.125 W).

Koivisto et al. (2000a) exposed right-handed healthy male (n = 24) and female subjects (n = 24) for 30 min to a 902 MHz RF EMF pulsed at 217 Hz during performance of a visual working memory task (N-back task; 0-, 1-, 2-, 3-back). Exposure or sham exposure occurred in a counterbalanced crossover design and was applied at the left side of the head. Accelerated response times were found for the target stimuli in the high memory load portion of the task (3-back). No EMF induced effects on accuracy of performance were observed. In a further study, Koivisto et al. (2000b) investigated the influence on cognitive performance under comparable exposure conditions by means of 12 different reaction time tasks. 24 male and 24 female subjects were exposed for 60 min to either the RF EMF or to the sham control condition in a randomized crossover design with a 24-h break between the two exposure conditions. Exposure was applied to the left side of the head. The RF EMF led to an acceleration of response times in the

simple reaction time task and the vigilance task as well as a decrease in mental subtraction time. Accuracy of performance was not affected except for a significant decline in false alarms during the vigilance task in the RF on condition. Both studies were performed single-blind.

A facilitation of processing speed was also shown by Edelstyn and Oldershaw (2002) who randomly assigned 38 healthy right-handed undergraduates to either a 900 MHz RF EMF with a SAR of 1.19 W/kg or to a sham control condition. In both groups, subjects held a mobile phone to their left ear for 30 min. Changes in cognitive performance were assessed by means of six different neuropsychological tasks applied immediately prior to mobile phone exposure (baseline), as well as 15 and 30 min after mobile phone exposure, respectively. Improvements in attentional capacity (digit span forwards, spatial span backwards) as well as in processing speed (serial subtraction) were observed after 15 min of exposure. The study was performed single-blind. It is not specified how many male and female subjects were participating. Especially with respect to the finding on spatial capacity the authors argue by means of the position of the antenna, which was mainly located in temporoparietal regions of the head. However, subjects had to hold the phone with their left hand to their left ear leading to inconsistent and not reproducible exposure conditions. In general, the exposure conditions and the dosimetry are not sufficiently described.

Lass et al. (2002) investigated the effects of a 450 MHz EMF modulated at 7 Hz on attention and short-term memory in three different neuropsychological tasks. 100 subjects (63 males) were randomly assigned to either an experimental group or a control group. Exposure or sham exposure of the right side of the head occurred during task performance (10-20 min). Response times and error scores served as a measure of cognitive performance in subjects who completed the tasks. The statistical analysis revealed a significant increase in errors in the modified “Trail making test B” and a test similar to the “Symbol Digit Modality test” under EMF exposure. In contrast, exposure decreased error scores in visual short term memory. The study was performed under single-blind conditions. The exposure duration was not fixed but stopped as soon as each subject finished the tasks. The number of subjects (males and females) used for statistical analysis is not explicitly stated. Possible sequence effects remained

unconsidered and the reported effects in the summary contradict the ones reported in the results section.

The study of Haarala et al. (2003b) was designed to replicate results previously obtained by Koivisto et al. (2000b) with improved methodology. By means of a double-blind design, a larger sample size, multicentre testing and additional cognitive tasks, the effects of a ~ 65-min 902 MHz left-side head exposure on cognitive performance was studied in 64 healthy subjects (32 males). Reaction time and accuracy of performance in nine different tasks served as behavioral variables to assess possible changes in brain functioning. The two exposure conditions (real and sham exposure) were separated by 24 h and the order was counterbalanced across subjects and gender. Contrary to Koivisto et al. (2000b), no significant effects were found in any of the tasks used. No gender differences or discrepancies between laboratories appeared. The results of the first study could not be replicated although reaction times and accuracy of the two studies did not differ remarkably. It is most likely that the replication has failed due to the improved study design. Moreover, it may be possible that the effects reported by Koivisto et al. (2000b) were detected by chance.

A study by Lee et al. (2003) investigated the effects of EMF exposure on attention in 78 right-handed undergraduate students randomly assigned to either the experimental group or the matched control group. Both groups completed two trials of cognitive tasks (~ 2 x 30 min) with a short break in between. Whereas the experimental group was exposed to the 1900 MHZ EMF during the first trial and sham exposed during the second one, the control group was never exposed. Exposure was applied to the right side of the head. Comparison of the exposed and the unexposed group with respect to performance measures (reaction time, accuracy of performance) revealed a stronger decrease in response times in the experimental group in one out of three neuropsychological tests (“Sustained attention to response task”). The study was performed under single-blind conditions. The exposure conditions and the dosimetry are not sufficiently described. It is not clear how many male and/or female subjects were participating. Apparently, no parallel test forms of the cognitive tasks were used. As the exposure conditions were not randomized (sham exposure always followed EMF exposure), sequence effects should be considered. Moreover, baseline performance in

the two study groups was not assessed. Therefore, it cannot be excluded that the performance of the two groups differed per se.

Smythe and Costall (2003) investigated the effects of mobile phone exposure (1800 MHz) on short- and long-term memory performance in 33 male and 29 female subjects. Stimuli were 12 single words arranged within a pyramid-shape ("Spatial word recall"). All subjects were randomly assigned to either a "no phone exposure" group, an "inactive phone exposure" group or an "active phone exposure" group. Subjects in the "active" and "inactive" phone group were exposed or sham exposed while holding a mobile phone with their left hand to their left ear. Exposure time added up to 15 min, comprising the acquisition phase (3 min) and a distraction task (12 min), in which the subjects had to read aloud passages from a newspaper. Subsequently, short-term recall was tested (3 min), in which subjects had to remember the correct position of the words in the pyramid as well as the words themselves. Approximately one week later, subjects returned for the retention and long-term recall phase of the same stimuli (3 min). Whereas no EMF induced effects were found in female subjects, results showed that males in the "active" phone condition made fewer spatial errors in the short-term recall than those in the "inactive" phone condition. No differences between the groups were observed in the retention phase. The study was performed single-blind. The exposure conditions and the dosimetry are not sufficiently described. With a total of 62 participants, the size of the groups varied across groups and gender. It is questionable if a standardized test was used to assess memory performance.

Besides the effects on cognitive performance, Curcio et al. (2004) investigated the time-course of electromagnetic field exposure on tympanic temperature. 20 subjects (50% males) were randomly assigned to two groups. Whereas the first group was exposed for 45 min prior to testing (left side of the head), the second group was exposed for the same amount of time during testing itself. Every complete test session lasted 90 min (45-min pre-recording, 45-min data recording). Three experimental conditions were applied in a double-blind counterbalanced order with 48 h in between: a baseline recording, a real exposure, and a sham exposure. A training session two days prior to the start of the experimental phase guaranteed comparable performance levels between subjects. During each session, performance in four different cognitive tasks was measured. Moreover, tympanic temperature was collected at five different time-points

distributed within 90 min. EMF exposure accelerated response times in an acoustic simple- and the choice reaction time task. Moreover, an increase in tympanic temperature was measured in the active field condition. The changes in these physiological measures appeared after a minimum of 25-min EMF exposure. No significant correlation between accelerated response times and increase in tympanic temperature was found.

Under similar methodological improvements as already mentioned (Haarala et al. 2003b), Haarala et al. (2004) were unable to replicate earlier findings observed in a verbal working memory task (N-back task, Koivisto et al. 2000a). Reaction times and accuracy of performance in 64 subjects (50% males) were assessed during a ~ 65-min exposure to a 902 MHz GSM EMF or a sham control condition. The exposure conditions were applied to the left side of the head and counterbalanced across subjects and gender in a randomized double-blind crossover design with a delay of 24±1 h in between. Statistical analysis revealed no significant differences in performance during EMF exposure. Besides the methodological improvements, the results are, however, difficult to compare as the type of N-back task and therefore the degree of difficulty in the two studies was not identical (letters of the whole alphabet vs. just ABCD).

Focusing on the long-lasting effects of constant daily exposure, Bessett et al. (2005) exposed a group of 28 subjects (2 h daily, five times a week) to an EMF while a second group of 27 subjects was sham exposed. Exposure conditions were applied to the left and the right side of the head and participants consisted of 27 males and 28 females. The study lasted 45 days and included a baseline period (3 days), an exposure period (28 days) and a recovery period (14 days). During recovery, all subjects were sham exposed. Neuropsychological assessment comprised 22 different tasks and was performed four times during the study, once during the baseline period, twice during the exposure period and on the last day of the recovery period. Statistical analysis revealed no alterations in performance speed in any of the tasks. The study was performed in a double-blind design. It is not clear how male and female subjects were distributed across the two study groups. The subjects held the mobile phone with their preferred hand to one ear, however, no information is given how many participants held the phone to which ear and if people were allowed to switch the exposed ear in the course of the study. In addition, exposure conditions are variable with respect to the exact location of

the mobile phone. With respect to the cognitive tasks, apparently no parallel test forms were applied, and therefore, learning effects cannot be excluded.

Haarala et al. (2005) examined the effects of a 50-min GSM exposure on cognitive performance in 32 children (10-14 years, 16 boys). Cognitive tasks were chosen based on previous experiments of the same group (Koivisto et al. 2000a; 2000b). In a double-blind design, each subject performed the tasks twice in two separate session (EMF off vs. EMF on) about ~ 24 h apart from each other. Active and sham exposure was applied to the left side of the head. In contrast to the results obtained in adults (Koivisto et al. 2000a; 2000b), no significant performance differences were found between the two exposure conditions. It is questionable if the results obtained can be compared to the ones reported by Koivisto et al. (2000a; 2000b) as performance in adults and children might not necessarily be comparable. No information is provided with respect to a training session prior to the experiment.

Likewise, Preece et al. (2005) reported no statistically significant differences in childrens' cognitive performance between active and sham RF EMF conditions. 18 children (10-12 years, 9 boys) participated in the experiment. Using the "Cognitive Drug Research" assessment system, modified to suit the children, three test sessions were applied after a training session in a randomized, double-blind crossover design. With few exceptions, test sessions were scheduled always at the same time of day on sequential days. The exposure conditions consisted of exposure to a 902 MHz GSM mobile phone emitting either 0 W, 0.025 W or 0.25 W mean output power. Exposure duration was 30 min and it was applied to the left side of the head. Although trends towards faster reaction times and higher accuracy scores were found during RF EMF exposure compared to sham exposure, none of the comparisons reached statistical significance. Therefore, the results reported previously could not be replicated (Preece et al. 1999). It should be stressed, however, that the exposure equipment and the exposure system differed between this study and Preece et al. (1999). Moreover, as already mentioned, performance in adults and children might not necessarily be comparable.

Using a new third generation like UMTS signal, Schmid et al. (2005) investigated the influence of a 1970 MHz mobile phone exposure on visual perception. In one 3.5-h

experimental session, four well established clinical tests were performed by each of the 58 subjects (50% males) during low (SAR_{10g} = 0.037 W/kg) and high-level exposure (SAR_{10g} = 0.37 W/kg) as well as sham exposure (50 dB below the low exposure condition) in a double-blind crossover design. Exposure conditions were applied to the left side of the head. Bonferroni corrected statistical analysis revealed no significant differences in the investigated parameters of visual perception between the exposure conditions and sham exposure. All tasks and conditions were performed in a row. No information is provided on the exact exposure duration. Moreover, it is not mentioned whether there was a break in between conditions. Therefore, fatigue as well as carryover effects cannot be excluded.

Eliyahu et al. (2006) attempted to establish a connection between 890 MHz GSM exposure of the ear region and the cognitive functions associated with this area. Spatial and verbal item recognition as well as two spatial compatibility tasks were performed during either left, right, or sham exposure. Within each exposure condition, subjects performed all tasks twice, once during the first 60 min and once during the second 60 min of exposure, with a 5-min break in between. Prior to the beginning of the first test, a 5-min training session was scheduled. Exposure conditions were counterbalanced, as was the sequence of tasks. All subjects were right-handed, however, reactions involved both hands. In the spatial item recognition task, exposure increased reaction times under left side RF EMF exposure only. This effect was observed in the second hour of exposure. A similar, however, not significant trend was observed in the verbal item recognition task and the spatial compatibility task. No results on accuracy of performance are provided. It is not clear whether the exposure conditions were all applied on one single day. In that case, carryover effects cannot be excluded. In general, the exact exposure duration is not well specified. Despite a counterbalanced design, the 5-min training session might have been too short to completely rule out learning effects. The screening for outliers appears to be chosen on a random basis (100 ms < reaction time < 3 s) and might have influenced data and subsequent data analysis.

A recent study by Keetley et al. (2006) revealed changes in cognitive performance after 60 min of RF EMF exposure in a study group of 58 male and 62 female subjects. Subjects began by completing a battery of eight psychological tests prior to exposure. Subsequently, a 30-min RF EMF or sham control exposure was applied in a double-blind

crossover design. The tasks were re-administered during the continuation of another ~ 30 min of exposure. The two conditions (real and sham exposure) were scheduled in distinct sessions approximately one week apart. Exposure conditions were applied to the left side of the head. During the sham control condition, the mobile phone was in a standby mode. Whereas accelerated response times under RF EMF exposure were observed in the “Trail making test B”, impairment in performance was found in four other tasks (“Audio visual learning task”, “Trail making task A”, “Simple and Choice reaction time task”). Exposure conditions and dosimetry are insufficiently described. Only uncorrected values are reported and an adjustment for multiple testing is lacking.

69 male and 99 female subjects participated in a study by Russo et al. (2006) who tested the effect of low level electromagnetic fields generated by mobile phones on human cognitive functions. In a sham controlled trial, the subjects performed four cognitive tasks previously applied in other studies (Haarala et al. 2003b; Koivisto et al. 2000b) in two different sessions one week apart from each other at the same circadian time. The sessions as well as the tasks were presented in a counterbalanced order. Dependent on the task, subjects had to response verbally (microphone) or motorically (keyboard). In the active field condition, half of the subjects was exposed to a GSM EMF while the other half was exposed to a continuous-wave EMF. Half of the exposure was performed on the left and on the right side of the heads, respectively. No effects of RF exposure or an interaction with gender or session was observed in any of the cognitive tasks. The study was performed double-blind. No information is provided with respect to the structure of the two study groups (e.g., males/females per group). Whereas (Koivisto et al. 2000b) used a key response, also verbal responses were measured by Russo et al. (2006), making a comparison between studies difficult. Exposure conditions and dosimetry are not sufficiently described.

Table 7: *RF EMF effects on cognitive performance (↑: significant increase; ↓: significant decrease; n.s.: no significant effect).*

Study	EMF Parameters [modulation in ()]	Sample size & Blinding	Measured variables	Results [compared to sham control]
(Preece et al. 1999)	Experiment 1+2: 915 MHz, analogue + pulsed (217 Hz), 1 W + 0.125 W mean net forward power; 25-30-min exposure, left side of head, phone fixed to ear	Experiment 1: n=18 subjects (9 males) Double-blind Experiment 2: n=18 subjects (9 males) Double-blind	Experiment 1+2: Immediate word recall	n.s.
			Picture presentation	n.s.
			Simple reaction time	n.s.
			Digit vigilance	n.s.
			Choice reaction time	↓ reaction times (analogue field)
			Spatial working memory	n.s.
			Numeric working memory	n.s.
			Delayed word recall	n.s.
			Delayed word recognition	n.s.
			Delayed picture recognition	n.s.
			(during exposure)	
(Koivisto et al. 2000a)	902 MHz (217 Hz), 577 µs pulse width, 0.25 W mean net forward power; 30-min exposure, left side of head, in 4 cm distance to head	n=48 subjects (24 males) Single-blind	N-back (0-, 1-, 2, 3-back)	↓ reaction times for target stimuli in the 3-back task
			(during exposure)	

Study	EMF Parameters [modulation in ()]	Sample size & Blinding	Measured variables	Results [compared to sham control]
(Koivisto et al. 2000b)	902 MHz (217 Hz), 577 µs pulse width, 0.25 W mean net forward power; 60-min exposure, left side of head, in 4 cm distance to head	n=48 subjects (24 males) Single-blind	Simple reaction time	↓ reaction times
			2-choice reaction time	n.s.
			10-choice reaction time	n.s.
			Subtraction	↓ subtraction time
			Sentence verification	n.s.
			Vigilance	↓ reaction times; ↓ false alarms
			Shape detection	n.s.
			Object detection	n.s.
			Object familiarity detection	n.s.
			Semantic picture categorization	n.s.
			Semantic word categorization	n.s.
			Object name retrieval task	n.s.
			(during exposure)	
(Edelstyn and Oldershaw 2002)	900 MHz, SAR=1.19 W/kg; 30-min exposure, phone with left hand to left ear	n=38 subjects Single-blind	Digit span forwards	↑ verbal memory capacity (after 15 min)
			Digit span backwards	n.s.
			Spatial span forwards	n.s.
			Spatial span backwards	↑ visuospatial working memory capacity (after 15 min)
			Serial subtraction	↑ sustained attention / processing speed (after 15 min)
			Verbal fluency	n.s.
			(before + after exposure)	

Study	EMF Parameters [modulation in ()]	Sample size & Blinding	Measured variables	Results [compared to sham control]
(Lass et al. 2002)	450 MHz (7 Hz), 50% duty cycle, 1 W output power SAR=0.0095 W/kg; 10-20-min exposure, right side of head, in 10 cm distance to skin	n=100 subjects (63 males) Single-blind	Modified trail making test B	↑ errors
			Visual short term memory	↓ errors
			Symbol digit modality test	↑ errors
			(during exposure)	
(Haarala et al. 2003b)	902 MHz (217 Hz), 577 µs pulse width, 0.25 W mean power, SAR_{1g}=0.88 W/kg (SAR_{peak}=1.2 W/kg); ~65-min exposure, left side of head, in 4 cm distance to surface of the skull	n=64 subjects (32 males) Double-blind	Simple reaction time	n.s.
			2-choice reaction time	n.s.
			10-choice reaction time	n.s.
			Subtraction	n.s.
			Sentence verification	n.s.
			Vigilance	n.s.
			Congruence task	n.s.
			Incongruence task 1	n.s.
			Incongruence task 2	n.s.
			(during exposure)	
(Lee et al. 2003)	1900 MHz (Nokia 3210); 30-min exposure, right side of head, phone oriented in normal position of use	n=78 subjects Single-blind	Trail Making Test A	n.s.
			Trail Making Test B	n.s.
			Sustained attention to response task	↓ reaction times
			(during exposure)	

Study	EMF Parameters [modulation in ()]	Sample size & Blinding	Measured variables	Results [compared to sham control]
(Smythe and Costall 2003)	1800 MHz, SAR=0.79 W/kg (Ericsson A2618s); 15-min exposure, phone with left hand to left ear	n=62 subjects (33 males) Single-blind	(Spatial) word recall (acquisition during exposure)	↑ spatial accuracy in male subjects
(Curcio et al. 2004)	902.4 MHz (217 Hz), 0.25 W mean power, SAR=0.5 W/kg (Motorola Timeport 260); 45-min exposure, left side of head, in 1.5 cm distance to ear	n=20 subjects (10 males) Double-blind	Acoustic simple reaction time task Visual search task Arithmetic descending subtraction task Acoustic choice reaction time task (during (group 1) + after exposure (group 2))	↑ speed (especially when exposed prior to test session) n.s. n.s. ↑ speed (target stimuli)
(Haarala et al. 2004)	902 MHz (217 Hz), 577 µs pulse width, 0.25 W mean power, SAR_{10g}=0.99 W/kg (SAR_{peak}=2.07 W/kg), (Nokia 6110); ~65-min exposure, left side of head, in ~4 cm distance to surface of the skull	n=64 subjects (32 males) Double-blind	N-back (0-, 1-, 2, 3-back) (during exposure)	n.s.

Study	EMF Parameters [modulation in ()]	Sample size & Blinding	Measured variables	Results [compared to sham control]
(Besset et al. 2005)	900 MHz (217 Hz), 576 µs pulse width, SAR=0.54 W/kg Exposure 2h/day, 5 x a week for 4 weeks, phone with preferred had to left and right side of head	n=55 subjects (27 males) Double-blind	Simple reaction time	n.s.
			Choice reaction time 1	n.s.
			Choice reaction time 2	n.s.
			Digit span forward	n.s.
			Spatial span forward	n.s.
			Modified Stroop task	n.s.
			Figure cancellation test	n.s.
			Auditory verbal learning test	n.s.
			Digit span backwards	n.s.
			Spatial span backwards	n.s.
			Number letter sequencing	n.s.
			Benton visual retention test	n.s.
			Purdue pegboard test	n.s.
			(before, during + after exposure)	
(Haarala et al. 2005)	902 MHz (217 Hz), 577 µs pulse width, 0.25 W mean power, SAR_{1g}=1.44 W/kg; SAR_{10g}=0.99 W/kg ~50-min exposure, left side of head, phone oriented in normal position of use	n=32 children (16 boys) Double-blind	Simple reaction time	n.s.
			2-choice reaction time	n.s.
			10-choice reaction time	n.s.
			Vigilance	n.s.
			N-back (0-, 1-, 2, 3-back)	n.s.
			(during exposure)	

Study	EMF Parameters [modulation in ()]	Sample size & Blinding	Measured variables	Results [compared to sham control]
(Preece et al. 2005)	902 MHz, a) 0 W power, b) 0.2 W peak power, c) 2 W peak power, SAR_{Brain}=0.28 W/kg (Nokia 3110); 30-min exposure, left side of head, phone oriented in normal position of use	n=18 children (9 boys) Double-blind	Word presentation	n.s.
			Immediate word recognition	n.s.
			Picture presentation	n.s.
			Simple reaction time	n.s.
			Digit vigilance	n.s.
			Choice reaction time	n.s.
			Spatial working memory	n.s.
			Numeric working memory	n.s.
			Delayed word recognition	n.s.
			Picture recognition	n.s.
			Dual attention task	n.s.
			(during exposure)	
(Schmid et al. 2005)	1970 MHz (5 MHz), a) High condition: SAR_{1g}=0.63 W/kg; SAR_{10g}=0.37 W/kg b) Low condition: 1/10 of High cond.; c) Sham: ≥50 dB below Low cond.; undefined exposure duration, left side of head, directly at the ear	n=58 subjects (29 males) Double-blind	Visual discrimination (Critical Flicker and Fusion Frequency Test)	n.s.
			Targeted and selective attention (Visual Pursuit Test)	n.s.
			Perceptive speed (Tachistoscopic Traffic Test Mannheim)	n.s.
			Contrast Sensitivity Threshold (CompuVist System)	n.s.
			(during exposure)	

Study	EMF Parameters [modulation in ()]	Sample size & Blinding	Measured variables	Results [compared to sham control]
(Eliyahu et al. 2006)	890.2 MHz, 577 µs pulse width, 2 W peak power, (Nokia 5110); 120-min exposure, left and right side of head, directly at the ears	n=36 subjects (males) Single-blind	Spatial item recognition task ("FACE")	↑ Reaction times with left hand (left side exposure, 2nd session)
			Verbal item recognition task ("LETTER")	n.s.
			Spatial compatibility ("SPAT")	n.s.
			Spatial compatibility ("SIMON")	n.s.
			(during exposure)	
(Keetley et al. 2006)	0.25 W mean power, (Nokia 6110); 60-min exposure, left side of head, antenna in 1.5 ±0.5 cm distance to head	n=120 subjects (58 males) Double-blind	Rey's audio visual learning test (AVLT)	↓ Performance (variable 7) ↓ Retrieval efficiency
			Digital span	n.s.
			Digital Symbol Substitution test (DSST)	n.s.
			Speed of comprehension test (SCT)	n.s.
			Trail making test (TMT A+B)	↓ Performance TMT A ↑ Performance TMT B ↑ Performance TMT difference
			Reaction time (RT)	↑ Reaction times
			Choice reaction time (CRT)	↑ Reaction times
			Inspection time (IT)	n.s.
			(before + during exposure)	

Study	EMF Parameters [modulation in ()]	Sample size & Blinding	Measured variables	Results [compared to sham control]
(Russo et al. 2006)	Exposure 1: 888 MHz GSM, SAR=1,4 W/kg (SAR_{peak}=11.2 W/kg); 35-40-min exposure, left or right side of head, antenna in direct contact to head Exposure 2: 888 MHz Continuous-wave, SAR=1,4 W/kg; 35-40-min exposure, left or right side of head, antenna in direct contact to head	n=168 subjects (69 males) Double-blind	Simple reaction time task 10-choice reaction time task Subtraction task Vigilance task (during exposure)	n.s. n.s. n.s. n.s.

EMPIRICAL PART

3 RESEARCH PROJECTS

3.1 Study I: Effects of Pulsed and Continuous-Wave Radio Frequency Electromagnetic Fields on Cognitive Performance and the Waking EEG

3.1.1 Introduction

The effects of radio frequency electromagnetic fields on cognitive-behavioral outcomes and the waking EEG are inconsistent and to some extent controversial. RF EMF were reported to influence cognitive functions such as working memory and attention during exposure (e.g., Koivisto et al. 2000a; Preece et al. 1999). The observed effects include facilitation and/or impairment of performance in distinct cognitive tasks (e.g., Curcio et al. 2004; Edelstyn and Oldershaw 2002; Keetley et al. 2006). In recent follow-up studies, however, some of the previously reported effects could not be corroborated (e.g., Haarala et al. 2003b; 2005; Krause et al. 2004; Preece et al. 2005). Except for Preece et al. (1999), all effects were observed in response to pulsed fields.

Pulsed RF EMF were also found to affect the waking EEG. Whereas Röschke and Mann (1997) did not detect any differences in spectral power in the waking EEG during a short exposure interval, Reiser et al. (1995) reported a 15-min delayed increase of EEG power in the alpha and beta band. Curcio et al. (2005) observed an increase of alpha power during and after exposure. In a previous study of our own lab we found that EEG power in the alpha and sigma range of the waking and sleep EEG was increased after pulse-modulated, but not after continuous-wave RF EMF exposure (Huber et al. 2002).

We aimed to corroborate the effects of RF EMF on brain functioning during waking and further elucidate the role of pulse modulation of RF EMF in mediating those changes. This is important because advanced telecommunication systems such as GSM include pulse modulation components (see chapter 1.7.1 and 1.7.2). We compared the effects of a pulse-modulated (PM) and a continuous-wave (CW) EMF on cognitive performance and the waking EEG. Based on previous studies (Koivisto et al. 2000a; 2000b; Preece et

al. 1999), we expected a shortening of reaction times in the cognitive tasks during exposure to both RF EMF conditions. Furthermore, we hypothesized that EEG alpha activity (8-12 Hz) would be increased after exposure to the PM signal, but not after exposure to the CW RF EMF (Huber et al. 2002).

3.1.2 Materials and Method

3.1.2.1 Study Participants

Twenty-four right-handed healthy male and non-smoking students (age range 19-25 years, mean 22.1±0.4 (± SEM)) with moderate alcohol (≤ 5 drinks per week) and caffeine (≤ 3 cups coffee per day) consumption participated in the experiment. They were recruited from the student population of the University of Zürich and ETH Zürich and were remunerated for participation. The local ethical committee for research on human subjects approved the study protocol. The subjects gave their written informed consent and reported to have no medical history of neurologic and psychiatric disease, to be in good health and not to take any medication or consume illicit drugs. Handedness was verified with the Edinburgh Handedness Inventory (Oldfield 1971). Six subjects did not own a cell phone, the remaining subjects reported to use it less than 1 h/week (mean use 36.7±3.0 min/week). On the three days before each experimental block, subjects were asked to abstain from caffeine, alcohol, and medication. They were instructed to adhere to a sleep-wake-schedule allowing 8 h of nighttime sleep (23.00-07.00 h, ±1 h with respect to bedtime) and not to nap during the day. Compliance with the instructions was verified by means of wrist-worn actimeters and sleep logs. Subjects were instructed to switch off their cell phone before going to bed on the night before each experimental block and to refrain from making calls until the experimental block was completed.

3.1.2.2 Study Design

The experiment consisted of three experimental blocks separated by one week. In each block, one of the following experimental conditions was applied in a double-blind, randomized and counterbalanced crossover design: exposure to (1) a PM RF EMF (see below), (2) a CW RF EMF (not modulated), and (3) sham exposure (no field). After a baseline (BL) EEG recording, subjects were exposed for 30 min while performing two

series of cognitive tasks. To investigate the time-course of RF EMF-induced effects on brain functioning, the waking EEG was recorded immediately after exposure, 30 min and 60 min after exposure. The experimental sessions were scheduled in the afternoon (between 14:45-18:00 h), always at the same time of day for a subject.

3.1.2.3 Exposure

Subjects were placed on a chair with their heads positioned between two planar antennas (for details on exposure setup and its dosimetry see Huber et al. 2003). Pairs of subjects were exposed unilaterally (left hemisphere) for 30 min to either an RF EMF or to the sham control condition. The two active exposure conditions comprised the same carrier frequency of 900 MHz and the same time-averaged power equivalent to a peak spatial SAR of 1 W/kg averaged over 10 g of tissue (exposure limit 2 W/kg). The PM signal simulated exposure from a GSM handset (bursts of 0.577 ms duration; modulation components of 2, 8, 217, 1733 Hz; see Huber et al. (2005) for details of signal). All electrode leads were horizontally oriented in order to minimize interference with the RF EMF in the active exposure conditions (Huber et al. 2003).

3.1.2.4 Cognitive Tasks

The following tasks were used to investigate RF EMF effects on cognitive functioning: "*Simple Reaction Time Task*" (SRT, Koivisto et al. 2000b), "*2-Choice Reaction Time Task*" (CRT, Preece et al. 1998) and "*N-Back Task*" (N-back, Koivisto et al. 2000a). We implemented the tasks using software from e-Prime (Psychology Software Tools Inc., Pittsburgh, PA, USA). In the SRT, a "0" was shown on the screen until the subject pressed the corresponding "0" button with the right index finger. In the CRT, either "*JA"* (yes) or "*NEIN"* (no) appeared on the screen and subjects had to press the corresponding "J" button with their right index finger or the "N" button with their right middle finger, respectively. In the N-back task, single consonants were randomly presented on the screen and subjects had to compare each current letter with any letter presented 1-, 2-, or 3-trials back. They had to respond to the targets (same letter) with their right index finger, and to non-targets (different letters) with their right middle finger, respectively (for a more detailed task description see also the Appendix). We instructed subjects to respond as quickly and as accurately as possible by pressing the

corresponding buttons on a response box. To assess possible changes that might occur during exposure, each task was presented twice in a fixed order (SRT, CRT, 1-, 2-, 3-back). Completion of one series of tasks took approximately 13-14 min and tasks were started by an experimenter. All subjects completed the tasks twice during the 30-min exposure interval. To ensure that subjects were well acquainted with the tasks and to reduce practice effects, subjects completed a training session seven days prior to the study.

3.1.2.5 Waking Electroencephalogram

The EEG (derivation C3A2), the EMG, the EOG (differential recording), and the electrocardiogram (ECG) were recorded by a polygraphic amplifier (PSA24, Braintronics Inc., Almere, The Netherlands), digitized, and transmitted via fiber-optic cables to a personal computer and stored with a resolution of 128 Hz (Rétey et al. 2006). Waking EEGs were recorded always for 6 min (3 min eyes closed, 3 min eyes open). Subjects were instructed to sit on a chair, to position their head on a chin support, and to move as little as possible. To minimize eye movements, subjects were instructed to slightly touch the closed eyelids with their index fingers (eyes closed) and to fixate a black dot on the opposite wall (eyes open). Vigilance was ensured by continuous on-line visual inspection of the EEG recordings. In case of any sign of drowsiness (e.g., rolling eyes, reduced alpha activity), subjects were immediately alerted via the intercom.

3.1.2.6 Statistical Analysis

Cognitive Tasks. Reaction times shorter than 50 ms were excluded as well as outliers over all sessions according to a robust rejection procedure (4 × median deviation, Hampel 1985). 3.6-6.7% responses were excluded (SRT: 6.7%; CRT: 3.6%; 1-back: 4.3%; 2-back: 5.7%, 3-back: 3.7%). Accuracy scores were not altered by this procedure. The reciprocal values of reaction times were expressed as speed (1/s; CRT and N-back: correct responses). Statistical analyses were carried out using linear mixed models (SAS 8.2, SAS Institute Inc., USA) presuming an identical intraclass correlation for all subjects (option “compound symmetry”). The model included the factors *Week* (1, 2, 3), *Condition* (sham, CW, PM), and *Session* (first and second half of exposure) as well as corresponding interaction effects. *Condition* was modeled as a categorical variable.

The percentage of correct answers in the CRT and the N-back task served as a measure of accuracy. Residuals were not normally distributed in the CRT and the 1- and 2-back task. Thus, non-parametric Wilcoxon-Signed-Rank tests were applied. Comparisons of CW vs. sham and PM vs. sham were performed for (i) session 1, (ii) session 2 and (iii) the difference between the two sessions (Δ). Significance levels were adjusted for multiple testing (6 tests) according to Bonferroni-Holm (Holm 1979). Residuals in the 3-back task approached a normal distribution and the data were analyzed with linear mixed models (compare speed analysis). Δ-values were analyzed in an overall model including the factor *Condition* (sham, CW, PM), *Load* (1, 2, 3-back) and the *Condition x Load* interaction. To control for multiple testing, a multiple endpoint adjustment was performed for the cognitive outcomes (Tukey et al. 1985).

Waking Electroencephalogram. The waking EEG was visually inspected for artifacts. Artifact-free EEG epochs of 2 s (at least 30 2-s epochs per recording) were subjected to spectral analysis (Hanning window; frequency resolution 0.5 Hz). Alpha activity was defined as activity in the frequency range between 8 and 12 Hz. Due to the high inter-individual variation of the position and size of the alpha peak, relative spectra were evaluated. For each subject, the position of the alpha-peak frequency was determined in the baseline spectra averaged over the three experimental conditions (sham, CW, PM). Spectra at 0, 30, and 60 min after exposure were centered at the alpha peak frequency of mean baseline (9.7±0.19 Hz) and expressed relative to the baseline of the corresponding condition. Log-transformed relative spectra (±5 Hz around the alpha-peak) were analyzed with linear mixed models. Two recordings were lost due to computer problems (30 min and 60 min after exposure, different subjects). The model included the factors *Week* (1, 2, 3), *Condition* (sham, CW, PM), *Time* (0, 30, 60 min after exposure) and the *Condition x Time* interaction. Post-hoc analyses comprised two-tailed paired t-tests.

3.1.3 Results

3.1.3.1 Cognitive Tasks

In the course of the study, subjects became slower in the SRT (*Week*: $p < 0.04$) and faster in the N-back tasks (1-, 2-, 3-back, *Week*: $p < 0.0001$). No change in speed over weeks occurred in the CRT. Irrespective of the exposure condition, speed decreased

from session 1 to session 2 in both the SRT and the CRT, but increased in the 2- and 3-back task (*Session*: $p < 0.001$). No difference between the two sessions was observed in the 1-back task. In the following, only effects including *Condition*, *Condition x Session* or *Condition x Load* interaction will be described.

Table 8: *Results of cognitive performance. Mean speed (1/Reaction time [1/s]; SEM in parenthesis; n = 24) in the two sessions (first and second half of exposure) in the SRT (Simple reaction time task), CRT (Two choice reaction time task), N-back task (1-, 2-, 3-back).*

Outcome	Session	Sham	CW EMF	PM EMF	Cond	Cond*Session
		mean (SEM)	mean (SEM)	mean (SEM)	p-value	p-value
SRT	1	4.01 (0.07)	3.97 (0.06)	3.94 (0.07)	0.12	0.71
	2	3.82 (0.07)	3.82 (0.07)	3.75 (0.07)		
CRT	1	2.57 (0.05)	2.57 (0.05)	2.56 (0.05)	0.83	0.90
	2	2.46 (0.05)	2.44 (0.04)	2.43 (0.05)		
1-Back	1	2.63 (0.10)	2.60 (0.10)	2.56 (0.09)	0.09	0.88
	2	2.70 (0.11)	2.63 (0.10)	2.61 (0.08)		
2-Back	1	1.88 (0.11)	1.81 (0.09)	1.74 (0.08)	0.0003	0.96
	2	2.03 (0.12)	1.94 (0.09)	1.89 (0.09)		
3-Back	1	1.62 (0.11)	1.66 (0.10)	1.51 (0.08)	0.0017	0.59
	2	1.77 (0.12)	1.73 (0.10)	1.64 (0.09)		

Whereas no RF EMF induced effect on speed was found in the SRT and the CRT, significant *Condition* effects were observed in the 2- and 3-back task ($p < 0.002$; 2-back: 1.95±0.11 1/s [sham], 1.87±0.09 1/s [CW], 1.81±0.08 1/s [PM]; 3-back: 1.70±0.11 1/s [sham], 1.70±0.09 1/s [CW], 1.58±0.08 1/s [PM], Table 8).

Accuracy was affected in the 3-back task only (Figure 5a; *Condition* x *Session* interaction, $p < 0.004$). An analysis of differences between the sessions (Figure 5b) revealed a *Condition* effect ($p < 0.001$) and a *Condition x Load* interaction ($p < 0.02$).

Thus, RF EMF dependent changes in accuracy were dependent on the cognitive workload, reaching significance in the 3-back task. After adjusting for multiple endpoints (α = 0.05; number of tests = 18; overall correlation among cognitive outcomes = 0.45), all observed *Condition* effects and the C*ondition* x *Session* interaction remained significant at the adjusted *p*-level of 0.01 (Tukey et al. 1985) but not the *Condition x Load* interaction.

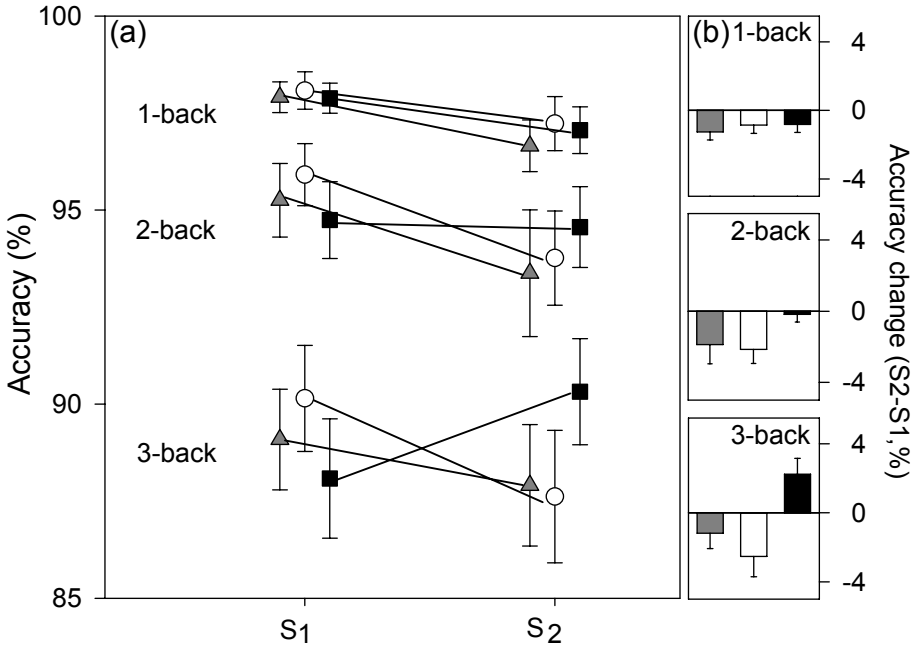

Figure 5: *Effect of RF EMF exposure on accuracy in the 1-, 2-, and 3-back task (mean ± SEM; n = 24). Three exposure conditions were applied: sham (▲) exposure, continuous-wave (○) and pulse-modulated (■) RF EMF exposure. (a) Accuracy in the first (S1) and the second (S2) half of exposure (session). Linear mixed model ANOVA revealed a significant Condition x Session interaction (p < 0.004) in the 3-back task. (b) Accuracy change from session 1 to session 2 (Δ). Linear mixed model ANOVA revealed a significant main effect for Condition (p < 0.001) and a significant Condition x Load interaction (p < 0.02). Gray bar sham, white bar continuous-wave, and black bar pulse-modulated RF EMF exposure.*

3.1.3.2 Waking Electroencephalogram

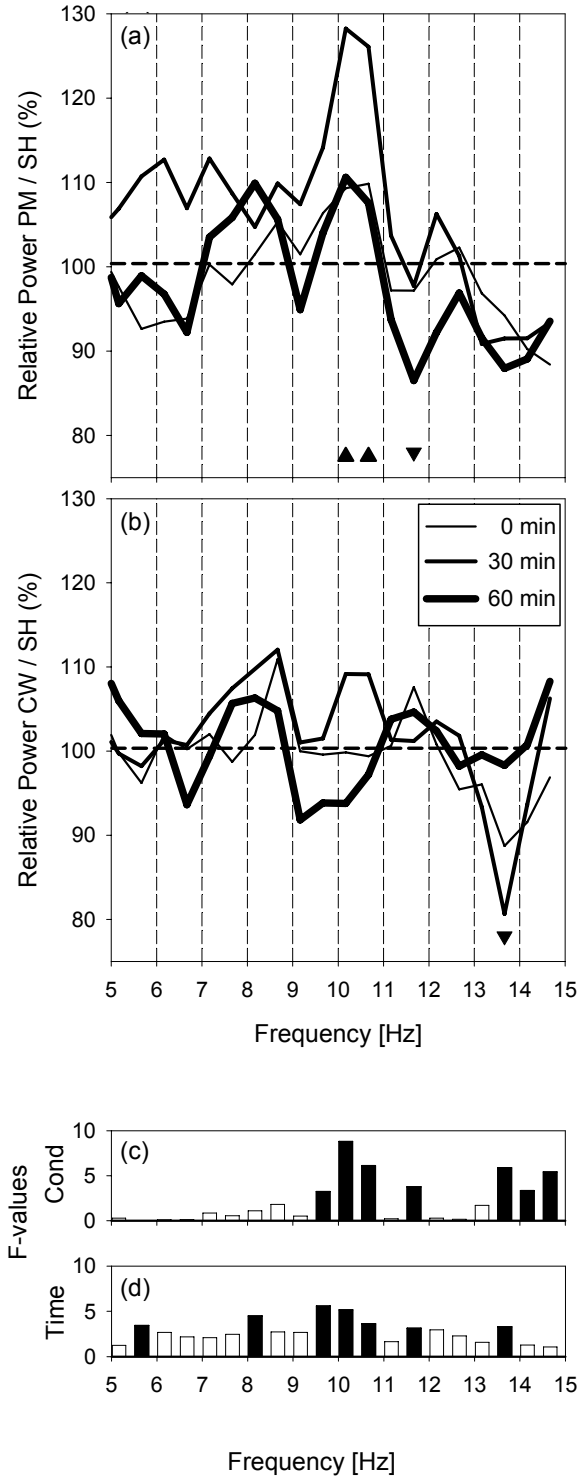

Figure 6: *RF EMF induced changes in the power spectra of the waking EEG (C3A2 derivation, eyes closed; n = 24) 0, 30 and 60 min after exposure. Power spectra were centred ± 5 Hz around the alpha peak frequency in baseline (9.7±0.19 Hz). Spectra in each condition were first expressed relative to the corresponding baseline and subsequently relative to the sham control condition (= 100%).*

SH: sham control condition.

CW: continuous-wave RF EMF;

PM: pulse-modulated RF EMF,

(a) Relative power spectra PM vs. SH; (b) relative power spectra CW vs. SH; (c) F-values of linear mixed model ANOVA for the factor Condition and (d) the factor Time. Significant values ($p < 0.05$) are indicated by black bars. Concomitant Condition and Time effects were post-hoc evaluated with two-tailed paired t-tests:

▲ *$p < 0.01$ PM vs. SH (30 min),*

▼ *$p < 0.03$ PM vs. SH (60 min),*
$p < 0.01$ CW vs. SH (30 min).

Exposure to PM RF EMF enhanced alpha power in the waking EEG (eyes closed) 30 min after exposure (Figure 6). Statistical analysis revealed significant main effects of *Condition* ($p < 0.05$) and *Time* ($p < 0.03$) between 10 and 11 Hz. Post hoc paired t-test revealed higher power in the 10.5 and 11 Hz bins 30 min after PM EMF exposure ($p < 0.01$) and lower power at 12 Hz 60 min after PM EMF exposure ($p < 0.03$) compared to sham control. No order effects were observed. The EEG of the eyes open condition was not reliably altered by RF EMF exposure.

3.1.4 Discussion

Our results indicate that pulse-modulated RF EMF similar to those emitted by mobile phones affect cognitive performance and the waking EEG at a peak spatial SAR of 1 W/kg. We observed a significant *Condition* effect on speed in the 2- and 3-back task. In the 3-back task accuracy was affected with increasing exposure duration, indicating that either an increased cognitive load or a certain exposure time is needed to induce an observable effect. Furthermore, the increase in alpha power was not observed immediately after exposure, but with a 30-min delay, indicating that these changes may outlast the exposure period.

Currently, no validated and reliable tool exists to asses cognitive effects of RF EMF exposure. The cognitive tasks applied in this study were chosen on the basis of recently published work (Koivisto et al. 2000a; 2000b; Preece et al. 1999). Based on the existing evidence, we conclude that RF EMF induced changes in cognitive performance are small and not all cognitive tasks are suitable or sensitive enough to reliably detect slight alterations in performance (see discussion in chapter 3.3.4). The effect on accuracy with increasing cognitive workload in the N-back task during PM EMF exposure suggests that RF EMF effects are only observed under a certain cognitive demand. This interpretation is consistent with the finding of Koivisto et al. (2000a) who reported improved performance in the high memory load portion of the N-back task only. In addition, not only the difficulty of a task but also the exposure duration prior to task performance may be relevant to observe an effect. In our experiment, all tasks were performed in two sessions and in a fixed order. Whereas no effects were observed in the first session, accuracy was affected in the second session of the N-back task only. As this task was always the last task in the whole sequence, exposure duration was the longest for this task. In contrast to our hypothesis we observed the changes in cognitive performance

during PM, but not during CW exposure supporting the relevance of PM in mediating RF EMF effects.

Increasing evidence indicates that pulsed RF EMF exposure affects alpha activity in the waking EEG (Croft et al. 2002; Curcio et al. 2005; D'Costa et al. 2003; Hinrikus et al. 2004; Huber et al. 2002; Reiser et al. 1995). RF EMF effects on alpha activity have been reported to occur during exposure as well as immediately after exposure (e.g., Curcio et al. 2005; D'Costa et al. 2003; Hinrikus et al. 2004). In our study, alpha activity was significantly increased 30 min after the end of PM RF EMF exposure, but not immediately after or 60 min after exposure, indicating that the effect appeared and disappeared within this time window. This finding is in line with Croft et al. (2002) who reported increased 8-12 Hz activity as a function of exposure duration. The interpretation of the reported alterations in oscillatory alpha activity is difficult. In general, the alpha rhythm dominates the human waking EEG in relaxed wakefulness. Yet, it shows high intra- and interindividual variation with respect to both frequency and amplitude (e.g., Klimesch 1999). Such inter-individual variation may depend on age, neurological status or memory performance (Klimesch 1999). The observed changes in spontaneous alpha activity may result from interference of RF EMF with electrophysiological properties of the brain, possibly inducing alterations in vigilance. The present findings confirmed our hypothesis that PM and not CW exposure affects alpha activity in the waking EEG.

Our results provide further evidence that pulse modulation is an important factor for RF EMF induced biological changes. However, the observed effects of pulse-modulated RF EMF on cognitive performance and brain activity were subtle and the underlying mechanisms remain unknown. Thus, the effects have to be interpreted cautiously in particular with respect to possible health consequences of RF EMF exposure.[◊]

[◊] Coinvestigators of this study were:

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3.2 Study II: Pulsed Radio Frequency Electromagnetic Fields: Dose-Dependent Effects on Sleep, the Sleep EEG and Cognitive Performance

3.2.1 Introduction

There is increasing evidence that pulse-modulated RF EMF such as emitted by mobile phones can affect brain physiology. The reported effects include changes in the EEG and regional cerebral blood flow as well as changes in intracortical excitability and cognitive function (e.g., Aalto et al. 2006; Borbély et al. 1999; Curcio et al. 2005; Ferreri et al. 2006; Huber et al. 2000; 2002; 2005; Koivisto et al. 2000a; 2000b). We recently found that pulse modulation of the RF EMF is necessary to induce changes in the EEG in waking and sleep (Huber et al. 2002, see also chapter 3.1). Exposure to a continuous-wave signal was not effective. Furthermore, a 'handset-like' signal had stronger effects on rCBF than a 'base station-like' signal (Huber et al. 2005).

So far, our previous experiments were carried out with a 10g-averaged peak spatial specific absorption rate ($psSAR_{10g}$) of 1 W/kg (Borbély et al. 1999; Huber et al. 2000; 2002; 2003; 2005). A dose-response relationship has not yet been established. We aimed to clarify this issue by using a five times lower and a five times higher SAR than in our previous studies. The investigation of the dose-response relationship is important for estimating the critical level for possible adverse health effects of RF EMF. We hypothesized that the sleep EEG and cognitive performance are affected in a dose-dependent manner by exposure to pulse-modulated RF EMF.

3.2.2 Materials and Method

3.2.2.1 Study Participants

Fifteen healthy young right-handed men (age range 20-26 years, mean age 22.4±0.4 (± SEM)) participated in the study. They were recruited from the student population of the University of Zürich and ETH Zürich and were remunerated for their participation. A screening night prior to the experiment served to exclude subjects with sleep apnea, nocturnal myoclonus and low sleep efficiency (< 80%). All subjects were non-smokers and reported to be in good health and free of sleep complaints. Handedness was verified with the Edinburgh Handedness Inventory (Oldfield 1971). Thirteen subjects reported to own a cell phone and to use it less than 1 h/week (32.5±2.3 min/week). They were instructed to abstain from caffeine and alcohol consumption at least 3 days prior to the study and to maintain a habitual sleep-wake schedule (8 h, 23:00-7:00 h ±1 h with

respect to bedtime). Compliance was verified with wrist-worn activity monitors and sleep logs. No mobile phone calls were allowed on the day of the experiment. Volunteers were informed that one of the exposure conditions was above the limit for the general population ($psSAR_{10g}$ of 2 W/kg, ICNIRP 1998) but still below the limit for occupational exposure ($psSAR_{10g}$ of 10 W/kg, see below). The subjects gave their written informed consent, and the local ethical committee for research on human subjects approved the study protocol.

3.2.2.2 Study Design and Exposure

The experiments were performed in the sleep laboratory of the Institute of Pharmacology and Toxicology, University of Zürich. The study consisted of three sessions separated by one-week intervals in a randomized double-blind crossover design. Each session consisted of an adaptation night and an experimental night (two groups with sleep either from 22:40-6:40 h or 23:20-7:20 h, respectively). In the experimental night, subjects were exposed unilaterally (left hemisphere) for 30 min prior to sleep to either a pulse-modulated RF EMF or to a sham control condition. The time between exposure and lights-off was 10 min. During exposure, subjects performed cognitive tasks while sitting in a chair with their head positioned between two plates to ensure a well-defined position with respect to the planar antennas (Huber et al. 2000; 2003). The setup allowed the simultaneous exposure of two subjects under the same condition. Hence, pairs of subjects were exposed together. The two exposure conditions involved a PM GSM-like handset signal (Huber et al. 2005, 900 MHz carrier frequency, burst of 0.577 ms duration, modulation components of 2, 8, 217 and 1736 Hz, duty cycle 12.3%) which was applied at a $psSAR_{10g}$ of either 0.2 W/kg or 5 W/kg.

3.2.2.3 Polysomnography

During the 8-h night-time sleep episodes the EEG (derivation C3A2), EMG, EOG (differential recording) and ECG were recorded with a polygraphic amplifier (PSA24, Braintronics Inc., Almere, The Netherlands), digitized, and transmitted via fiber-optic cables to a personal computer and stored with a resolution of 128 Hz (Endo et al. 1998).

3.2.2.4 Cognitive Tasks

Based on previous experiments, the following tasks were used to assess the influence of RF EMF exposure on cognitive performance: SRT, CRT (Koivisto et al. 2000b; Preece et al. 1998) and N-back Task (1-, 2-, 3-back, Koivisto et al. 2000a, see also chapter 3.1.2.4 and the Appendix). The tasks were implemented using e-Prime (Psychology Software Tools Inc., Pittsburgh, PA, USA). After a training session on the first adaptation night, subjects performed the tasks during exposure while sitting in the exposure setup about 1 m in front of a flat panel monitor. SRT, CRT and 1-, 2-, and 3-back task were performed twice in a fixed order, once during the first half and once during the second half of exposure (sessions 1 and 2). Subjects were instructed to respond as quickly and as accurately as possible to targets and non-targets by pressing the corresponding buttons on a response box.

3.2.2.5 Statistical Analysis

Polysomnography. Sleep stages were visually scored for 20-s epochs according to standard criteria (Rechtschaffen and Kales 1968). EEG power spectra of consecutive 20-s epochs (FFT routine, Hanning window, averages of five 4-s epochs) were computed (Borbély et al. 1999; Huber et al. 2000; 2002) and visual and semi-automatic artifact removal was performed (Huber et al. 2000). Due to electrode problems and associated loss of data at the end of the night, analysis of power spectra between 0 and 20 Hz was restricted to the minimal common length of 905 x 20-s epochs (~ 300 min). Average power spectra of stage 2 non-REM sleep (log-transformed values) were analyzed with linear mixed models including the factors *Week* (1, 2, 3, to account for order effects) and *Condition* (sham, 0.2 W/kg, 5 W/kg). The factor *Condition* was modeled as a continuous variable. Statistical analysis revealed a trend for the main factor *Condition* in the spindle frequency range (13.5-14 Hz). Therefore, additional analyses were performed with the 13.5-14.0 Hz band and log-transformed values of three consecutive intervals of 100 min were analyzed by expanding the mixed model with the factor *Interval* (1, 2, 3) and the *Condition* x *Interval* interaction. In addition, linear mixed model ANOVA was performed with sleep variables derived from visual scoring.

***Cognitive Tasks*.** Reaction times shorter than 50 ms were excluded and a robust rejection-estimation procedure (4 x median deviation, Hampel 1985) served to exclude individual outliers over all sessions. Ultimately, 4.4-6.6% responses were excluded (SRT: 6.6%; CRT: 4.4%; 1-back: 5.6%; 2-back: 5.5%, 3-back: 5.2%). Accuracy scores were not altered by this procedure. The residuals of the transformed reaction times (speed: 1/reaction time) fulfilled criteria of a normal distribution. Obtained speed values [1/s; correct responses only] were analyzed with linear mixed models (SAS 8.2, SAS Institute Inc., USA) presuming an identical intraclass correlation for all subjects (option "compound symmetry"). The model included the factors *Week* (1, 2, 3), *Condition* (sham, 0.2 W/kg, 5 W/kg), and *Session* (first and second half of exposure) as well as the *Condition* x *Session* interaction. The factor *Condition* was modeled as a continuous variable.

Accuracy of performance (percentage of correct answers) in the CRT and the N-back task were statistically analyzed by non-parametric Wilcoxon-Signed-Rank tests. Comparisons of 0.2 W/kg vs. sham and 5 W/kg vs. sham were performed for (i) session 1, (ii) session 2 and (iii) the difference between the two sessions (Δ). Significance levels were adjusted for multiple testing (six tests) according to Bonferroni-Holm (1979). For the cognitive outcomes a multiple endpoint adjustment was performed to control for multiple testing (Tukey et al. 1985).

3.2.3 Results

3.2.3.1 Sleep and Sleep Electroencephalogram

If not indicated, only significant effects are reported.

Sleep architecture was not affected by RF EMF exposure (Table 9). Sleep latency (interval from lights off to stage 2 sleep) tended to be slightly prolonged with increasing field intensity (*Condition*: $p < 0.06$, Table 9). No other dose-response related effects emerged.

Table 9: *Sleep variables derived from visual scoring for the three experimental conditions: sham condition, pulse-modulated RF EMF with a 10 g-averaged peak spatial SAR of 0.2 W/kg and 5 W/kg. All-night means in min (SEM in parenthesis; n = 15). Sleep latency: Interval from lights off to stage 2 sleep. REM sleep latency: Interval from sleep onset (stage 2) to the first occurrence of REM sleep. Slow-wave sleep: NREM sleep stages 3 and 4.*

	Sham mean (SEM)	**SAR 0.2 W/kg mean (SEM)**	**SAR 5 W/kg mean (SEM)**
Time in bed	479.2 (0.5)	479.9 (0.0)	479.9 (0.0)
Total sleep time	449.2 (2.9)	445.0 (4.5)	444.5 (3.6)
Sleep latency	16.9 (2.9)	19.4 (2.4)	20.7 (2.8)
REM sleep latency	65.8 (4.9)	67.3 (4.9)	71.8 (5.9)
Waking after sleep onset	3.8 (1.2)	5.2 (2.6)	3.6 (0.9)
Stage 2	270.6 (9.2)	268.5 (7.2)	267.3 (7.7)
Slow wave sleep	59.4 (6.0)	60.4 (5.5)	58.0 (5.7)
REM sleep	92.1 (4.2)	83.1 (5.2)	87.7 (3.5)
Movement time	9.3 (0.8)	9.6 (0.7)	9.9 (1.2)

Spectral analysis of the sleep EEG in stage 2 revealed a trend of a dose-dependent increase of power in the spindle frequency range after pulse-modulated RF EMF exposure (Figure 7). The increase was 7.7% after RF EMF exposure with 0.2 W/kg and 13.6% after exposure with 5 W/kg (Figure 7). The temporal evolution of the effect in the spindle frequency range (13.5-14 Hz band) was analyzed for the first three 100-min intervals (Figure 8). Statistical analysis revealed a significant *Condition* effect ($p < 0.04$), which was not limited to a specific time interval but was present the entire sleep episode (Figure 8; *Condition x Interval*: $p < 0.9$). Post-hoc analysis comparing each exposure condition with the sham condition separately (0.2 W/kg vs. sham; 5 W/kg vs. sham) revealed that the 5 W/kg condition differed significantly from the sham control condition (*Condition*: $p < 0.05$).

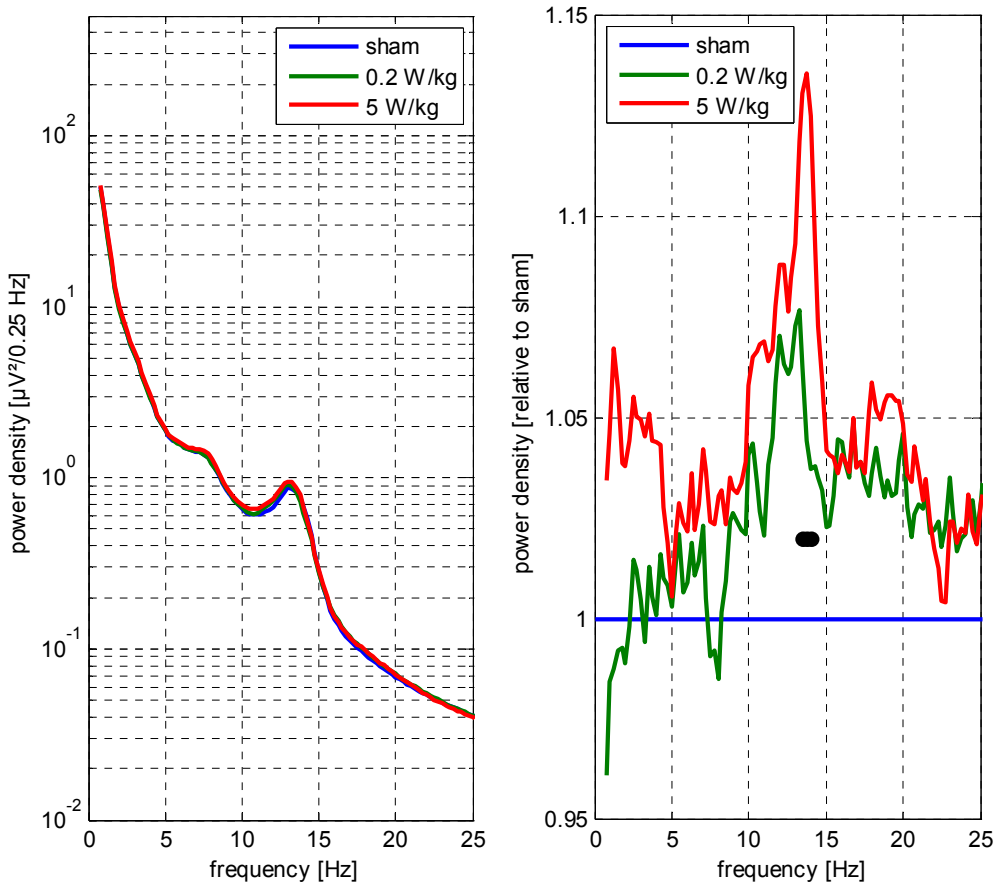

Figure 7: *Dose-dependent effect of RF EMF exposure on EEG power spectra in stage 2 non-REM sleep (derivation C3A2). Absolute (left panel) and relative (right panel) EEG power density spectra (n = 15, sham = 1 (= 100%)) are illustrated. Three conditions were applied: sham exposure, 0.2 W/kg and 5 W/kg RF EMF exposure (10 g averaged peak spatial SAR). Linear mixed model ANOVA factor Condition revealed a trend in the spindle frequency range (13.5-14 Hz; ● 13.5 Hz bin: p = 0.07; 13.75 Hz bin: p = 0.06; 14.0 Hz bin: p = 0.09; Week: 13.5-14 Hz, p < 0.03).*

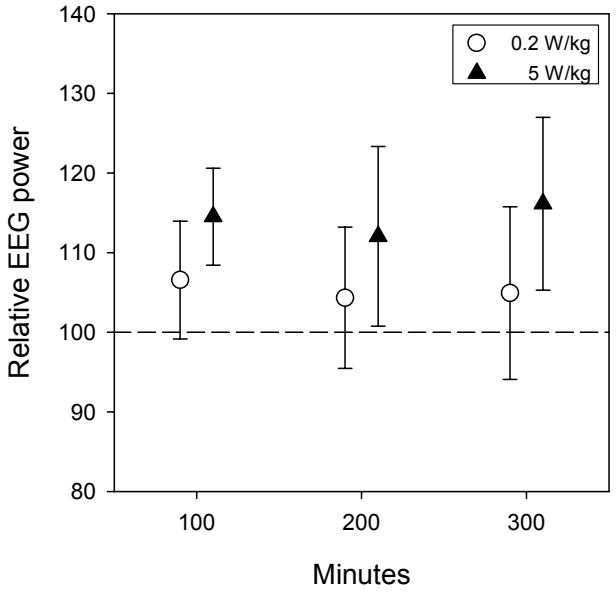

Figure 8: *Temporal evolution of the effect of RF EMF exposure on spindle frequency activity (13.5-14 Hz). Three conditions were applied: sham, 0.2 W/kg and 5 W/kg RF EMF exposure (10 g-averaged peak spatial SAR). Relative EEG power (sham = 100%) was increased in a dose-dependent manner in the first three 100-min intervals (n = 15; linear mixed model ANOVA, factor Condition: p < 0.04; Condition x Interval interaction: p < 0.9).*

3.2.3.2 Cognitive Tasks

All subjects completed the tasks during the 30-min exposure interval. In the course of the experiment, subjects became faster in the N-back task (1-, 2-, 3-back, *Week*: $p < 0.001$). No changes in speed over the experimental period were observed in the SRT and the CRT. Irrespective of exposure condition, speed decreased significantly from session 1 to session 2 in both the SRT and the CRT, but increased in the 1- and 2-back task (*Session*: $p < 0.03$). No significant difference between the two sessions was present in the 3-back task. If not indicated, only significant effects are reported in the following.

Speed significantly decreased with increasing field intensity in the 1-back task (*Condition*: $p < 0.004$) and a similar trend was observed for the CRT and the 2-back task

(CRT: $p < 0.09$; 2-back: $p < 0.07$; Figure 9). No RF EMF induced effect on speed was found in the SRT and the 3-back task. In general, no difference in speed was observed between the first and the second half of exposure (*Condition x Session*: $p > 1.0$). Accuracy was not affected in a dose-dependent manner in any of the tasks applied. In the first session of the 2-back task statistical analysis revealed a difference between accuracy scores of the 0.2 W/kg condition compared to the sham control condition ($p < 0.003$), but not of the 5 W/kg condition ($p < 0.4$). Subjects performed worst during the sham condition (93% correct responses) and best during the 0.2 W/kg condition (96% correct responses) with performance during 5 W/kg ranging in between (95% correct responses).

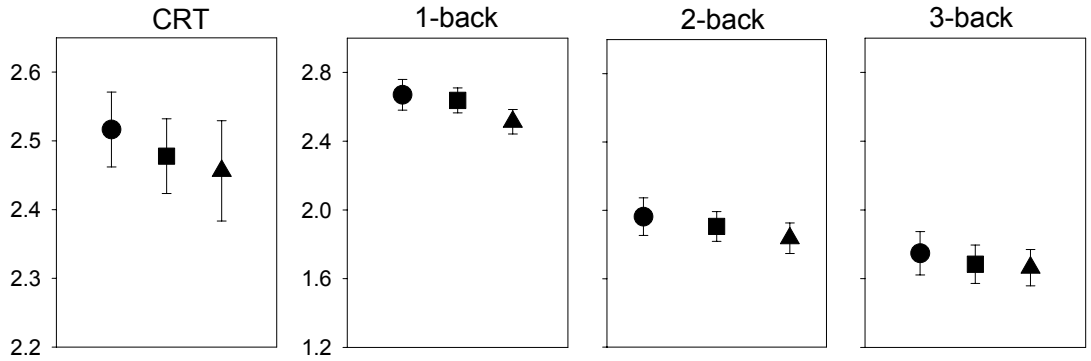

Figure 9: Dose-dependent effect of RF EMF exposure on speed (1/reaction time, mean ± SEM; n = 15) in the CRT (Two choice reaction time task) and N-back task (1-, 2 -, 3-back). Three conditions were applied: sham (●), 0.2 W/kg (■), and 5 W/kg (▲) RF EMF exposure (10 g-averaged peak spatial SAR). CRT: $p < 0.09$; 1-back: $p < 0.004$; 2-back: $p < 0.07$; 3-back: $p < 0.4$; factor *Condition*, linear mixed model ANOVA.

3.2.4 Discussion

Our data indicate a dose-dependent effect of pulsed RF EMF exposure on the non-REM sleep EEG and cognitive performance in humans. In contrast to cognitive performance, sleep EEG recordings in a controlled environment constitute a more reliable method to assess the effects of RF EMF exposure, because spectral power is largely independent of motivational aspects and alterations in vigilance. Consistent evidence accumulates that pulse-modulated RF EMF exposure affects the non-REM sleep EEG in the alpha

and sigma range (present study, Borbély et al. 1999; Huber et al. 2000; 2002; 2003; Loughran et al. 2005). In agreement with Huber et al. (2002), the increase of power after handset-like RF EMF exposure (see Huber et al. 2005 for signal characteristics) was limited to the spindle frequency range. In conjunction with previous findings (Huber et al. 2002), our data provide evidence for a dose-response relationship: spindle frequency activity increased by 7.7 % after RF EMF exposure with 0.2 W/kg, 10% after exposure with 1 W/kg (Huber et al. 2002), and 13.6% after exposure with 5 W/kg. In our study, the increase of spindle frequency activity was at a similar level throughout the sleep episode (Figure 8), whereas Huber et al. (2002) reported an increase of the effect in the course of sleep that paralleled the increase of spindle activity. Bi- or unilateral exposure of the cortex caused changes in the sleep EEG of both hemispheres (Huber et al. 2000; 2003). Because the effect did not depend on the side of exposure, we hypothesized that the lower dose present at the non-exposed hemisphere may have been sufficient for a maximal effect. This interpretation, however, is not supported by our present findings of a dose-dependent effect. In agreement with previous findings (Huber et al. 2000; 2002; Wagner et al. 1998; 2000), we did not observe any changes in sleep architecture after RF EMF exposure.

In three out of five cognitive tasks speed tended to decrease during exposure to PM RF EMF in a dose-dependent manner, reaching significance in the 1-back task. No dose-response relationship was found for accuracy. Surprisingly, subjects performed best in the 2-back task in the first half of the 0.2 W/kg exposure condition. This is in contrast to our previous finding (chapter 3.1.3.1) where accuracy increased during exposure with a pulse-modulated EMF of 1 W/kg in the 3-back task. So far, several studies have reported effects of RF EMF on cognitive functions. However, cognitive performance does not seem to be consistently affected and recent studies have failed to corroborate previous findings (Haarala et al. 2003b; 2004; Krause et al. 2004; Preece et al. 2005). Such inconsistencies may be due to the lack of standardized and validated cognitive tasks to assess effects of RF radiation as well as to the large differences with respect to exposure setup, exposure conditions and study design (see discussion in chapter 3.3.4). Alternatively, in several studies including our own, statistical power may have been insufficient to reliably detect RF EMF induced changes on cognitive functioning. Generally, cognitive performance may be influenced by a variety of factors (e.g., motivation, distraction, boredom etc.) and a sufficiently high sample size might be needed to compensate for the high intra- and inter-individual variability.

In conclusion, evidence is increasing that RF EMF exposure prior to sleep may alter brain activity. Our study results indicate a dose-response relationship of RF EMF exposure for the non-REM sleep EEG and cognitive performance. It can be assumed that the changes we observed were non-thermal as pulse-modulated handset-like RF EMF, but not continuous-wave RF EMF was shown to affect the EEG during sleep at the same $psSAR_{10g}$ of 1 W/kg (Huber et al. 2002). Moreover, it is not likely that a thermal effect would last up to 5 h after termination of exposure. ◊

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Supported by the Swiss National Science Foundation, the Research Foundation Mobile Communication and the Federal Office of Public Health.

3.3 Study III: UMTS Base Station-Like Exposure, Well-being and Cognitive Performance

3.3.1 Introduction

In 2003 a Dutch study on the effects of controlled exposure to mobile communication system RF EMF at base station intensities on human well-being and cognitive function was published (TNO study, Zwamborn et al. 2003). Effects of two systems were explored: the second-generation Global System for Mobile Communication widely used around the world, and its successor, the Universal Mobile Telecommunications System, the third generation of mobile networks. Two groups of subjects were investigated, consisting of individuals with and without self-reported health complaints attributed to daily life exposures to RF EMF. Although exposure to GSM-like EMF had no effect at the time-averaged incident E-field strength of 0.7 V/m, UMTS-like exposure at an E-field strength of 1 V/m reduced well-being in both groups. No consistent effects on cognitive performance were found. The 3 dB difference of the averaged incident fields was unlikely to have contributed to the different outcome of GSM and UMTS exposure on well-being. The results were hypothesized to be due to the different modulation schemes. The TNO study was the first to investigate a base station-like exposure and to indicate a reduction in well-being. Regarding the stronger but much more localized exposure by mobile phone handsets, there is an abundant yet controversial body of research on potential nonthermal effects on humans. Data on well-being are inconclusive (Rubin et al. 2006; for a review see Seitz et al. 2005), yet various studies identified subtle effects regarding changes in brain activity or influences on cognitive function such as reaction times, working memory, and attention (e.g., Curcio et al. 2005; Freude et al. 2000; Huber et al. 2002; 2005; Hyland 2000; Koivisto et al. 2000b; Krause et al. 2000a). Some of the reported changes (e.g., acceleration of response times in certain cognitive tasks, altered oscillatory activity in the electroencephalogram as a function of time and task), however, were inconsistent and could not be replicated (Haarala et al. 2003b; Krause et al. 2004; Preece et al. 2005). An ongoing debate in RF EMF research and the general public concerns self-reported electromagnetic hypersensitivity relating to persons attributing subjective complaints of impaired well-being (e.g., headache, nausea, sleep disturbances) to EMF exposure comprising radio frequency as well as extremely low frequency fields of domestic power supplies (e.g., National Institute of Environmental Health Sciences - NIEHS Working Group Report 1998; Röösli et al. 2004). To date, no causal link has been found between exposure to

mobile phones and EHS symptoms (for a review see Rubin et al. 2005), and objective criteria for EHS specification could not be established. The persisting uncertainty associated with potential adverse health effects of the new UMTS technology, together with its rapidly ongoing implementation, has led to widespread public concern in many countries. We designed the present experiment as a follow-up study to clarify the reliability of the TNO study that was largely debated in the scientific community. We used validated measuring instruments and an improved setup yielding better uniformity of exposure, as well as an additional E-field strength (10 V/m) to establish a dose-response relationship. Based on the results reported by Zwamborn et al. (2003), we hypothesized that exposure to UMTS-like radiation would attenuate subjective well-being in both sensitive and nonsensitive subjects, possibly in a dose-dependent manner, but would not affect cognitive performance.

3.3.2 Materials and Method

3.3.2.1 Study Participants

We investigated the effects of UMTS-like EMF in subjects with self-reported sensitivity to RF EMF ($n = 37$) and a reference group without complaints ($n = 91$). Because of noncompliance of three subjects and eight dropouts, the final study group included $n = 33$ sensitive (14 males, 19 females) and $n = 84$ nonsensitive subjects (41 males, 43 females). Both groups were recruited from the general public by advertisement in a local newspaper, by flyers, and from databases of two previous studies with sensitive participants willing to participate in future research projects. Because of a lack of an operational tool for measuring sensitivity to EMF (World Health Organization 2005), criteria for recruitment were based on self-reported sensitivity to RF EMF, that is, purported sensing of RF EMF or afflictions related to RF EMF as emitted by mobile or cordless phones and antennas. Subjects were contacted by telephone and preselected by a standardized interview. Exclusion criteria comprised pacemakers, hearing aids, artificial cochleas, regular consumption of narcotics or psychoactive drugs in the previous 6 months, smoking, polymorbidity with respect to chronic diseases, pregnancy, a medical history of head injuries and or neurologic/psychiatric diseases, sleep disturbances, and an average consumption of alcohol > 10 drinks/week or of caffeinated beverages amounting to > 450 mg caffeine/day (e.g., approximately three cups of coffee). We also excluded shift workers and persons undertaking long-haul flights (> 3 h

time zone difference) within the last month before the experiment. On their first appointment, all subjects filled in a questionnaire to verify the exclusion and matching criteria (age in decades, sex, and residential area). The entire reference group was frequency matched to the sensitive group, and a subgroup was 1:1 matched, also including body mass index (BMI). Subjects were between 20 and 60 years of age (mean±SD, 37.7±10.9), right-handed (Oldfield 1971), and of normal body weight (BMI 19-30 kg/m^2). They gave their written informed consent and were reimbursed for participating. The cantonal ethical committee of the Canton Zürich approved of the study protocol.

3.3.2.2 Study Design

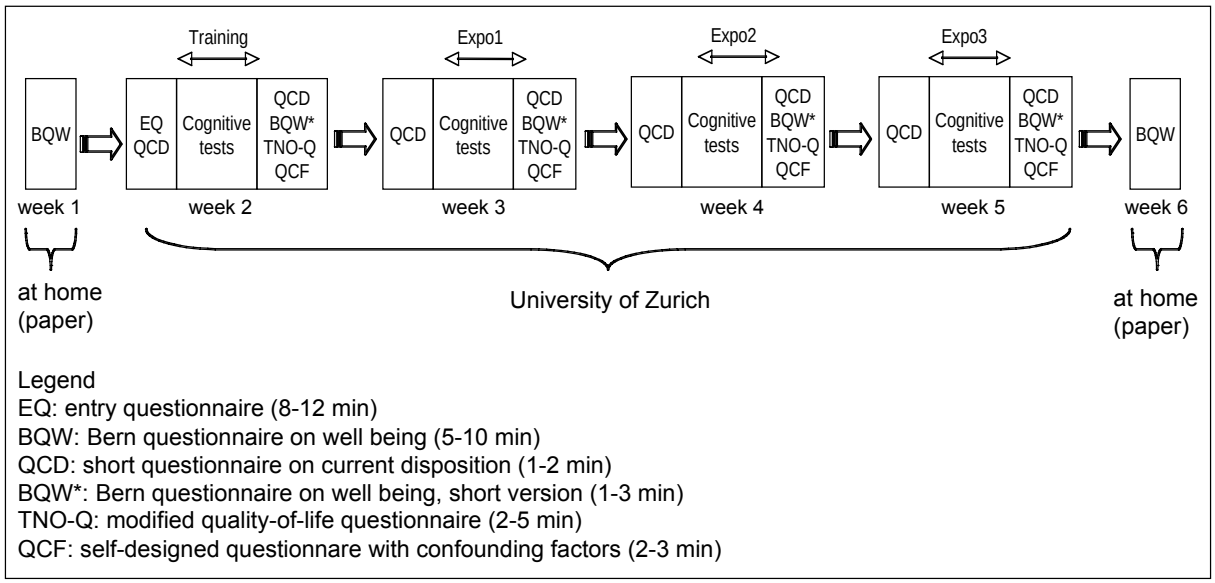

Figure 10: *Overview of the experimental design and the questionnaires applied (see also chapter 3.3.2.4).*

We performed the study at the Institute of Pharmacology and Toxicology, University of Zürich, between 1 February and 20 May 2005. It consisted of three experimental sessions at one-week intervals (±1 day) that were preceded by a training session 7±1 days ahead and that were always scheduled at the same time of day (~ ±2 h). Subjects were evenly distributed across experimental period, weekdays, and time of day. We asked them to abstain from any medication 24 h before each session and also

requested them not to use a mobile or cordless phone for 12 h preceding the sessions. Exposure was computer controlled providing double-blind conditions, which we applied in a randomized crossover design. Before and after exposure, subjects filled in the questionnaires in an office room and were then escorted to the exposure chambers. Exposure took place in two identical and specially adapted but separate rooms with constant temperature and light conditions. We randomly assigned pairs of subjects to one of six possible sequences of the three exposure conditions [0 (sham), 1 V/m, 10 V/m] but shifted the subjects in each pair by 20 min to minimize contact between them. Each exposure session lasted 45 min, during which subjects performed two series of cognitive tasks (sessions 1 and 2), starting at the beginning and after 22 min of exposure, respectively. Between sessions, subjects remained in front of the computer and were allowed to read magazines.

3.3.2.3 Exposure and Dosimetry

Each experimental room included an exposure area installed as a one-side-open chamber shielded with RF radiation absorbers (Figure 11). We placed the antenna (SPA 2000/80/8/0/V; Huber & Suhner, Herisau, Switzerland) at 1.5 m height and 2 m distance from the subjects, targeting the left side of the body from behind, with a field incidence angle of 25° with respect to the ear-to-ear vertical plane (Figure 11). To produce the same polarization as in the TNO study, we tilted the antenna and thus the E-field 45° from vertical. The antenna possessed a –3-dB beam width of approximately 75° in horizontal and vertical directions, resulting in a uniform E-field distribution in a manner similar to that of the far field of a base station.

We verified field uniformity before and after the experimental phase by scanning the exposure area with a field probe. The UMTS signal format was identical to the one used by Zwamborn et al. (2003), consisting of four control and synchronization channels (primary synchronization channel, –8.3 dB below total RF power; secondary synchronization channel, 8.3 dB; primary common control physical channel, –5.3 dB; common pilot channel, –3.3 dB) with a center frequency of 2,140 MHz and chip rate of 3.84 microchips/s. The signal, generated by a commercial generator (E4433B Options 200, 201, UN8, UN9; Agilent Technologies, Palo Alto, CA, USA), corresponded to a UMTS base station frequency division duplex mode downlink configuration with no active voice calls. Exposure was continuously monitored and regulated (three-axis E-field

probe). Each chamber was equipped with a wooden table and chair, a flat-panel monitor with keyboard, a plastic response box for the cognitive tasks, and the UMTS antenna with a field probe (Figure 11).

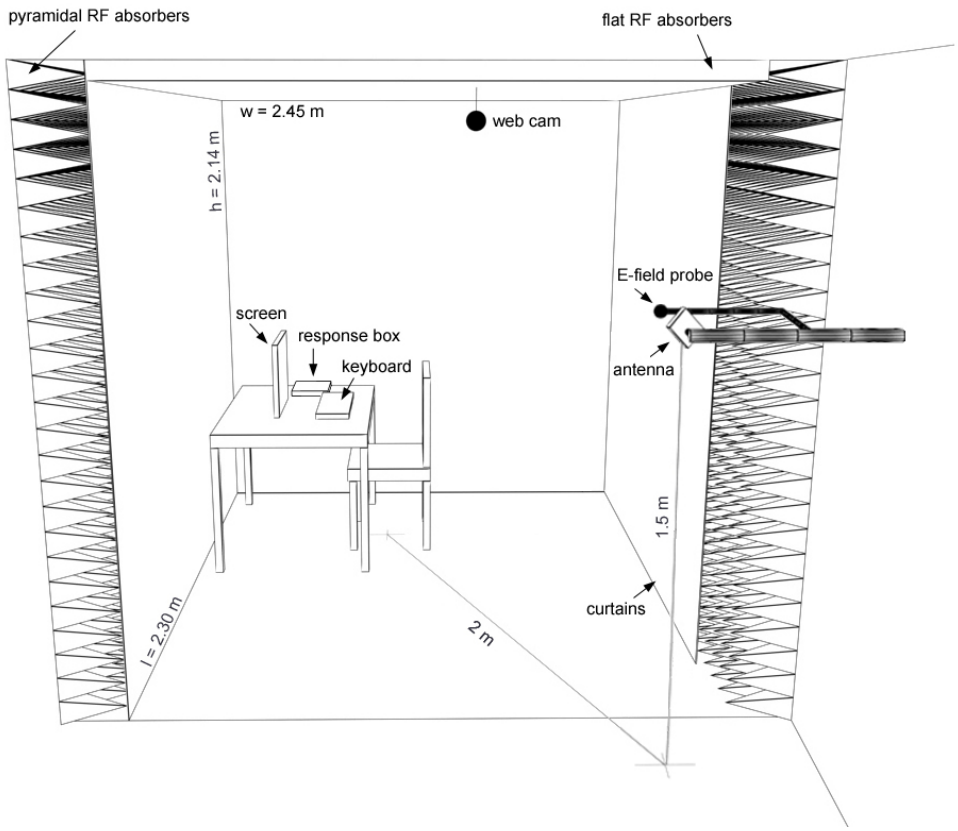

Figure 11: *Sketch of the exposure chamber. Walls were covered by pyramidal RF absorbers and nonreflecting curtains. The ceiling was covered by flat absorbers. Antenna, E-field probe, furniture, screen keyboard, response box, web camera, inner dimensions (w: width; h: height; l: length), and position of the antenna are indicated.*

The web camera that recorded the subjects from top left (1 frame/s) and the computer hardware were outside the exposure chamber. The sum of all magnetic fields (frequency range, 30 Hz-400 kHz) was below 0.2 μT. We measured background RF radiation levels (80 MHz-4 GHz) before and after the experiment, and they remained below 1 mV/m over the whole exposure area. We conducted numerical dosimetry according to Kuster and Schönborn (2000) using the finite-difference time-domain simulation platform Semcad X (SPEAG, Zurich, Switzerland) and three whole-body anatomical phantoms (two male, one female). We treated reflections from furniture as uncertainty, reducing the

computational space to 2.6 x 1 x 1.8 m^3 (length x width x height). We modeled the floor as concrete (i.e., relative permitivity of 7.5, and conductivity of 0.12 Siemens per meter), whereas the walls and ceiling were modeled as perfectly absorbing boundaries. The numerical discretization of the chamber was 5 x 5 x 5 mm^3, of the human model 2 x 2 x 2 mm^3, and of parts of the antenna 1 x 0.5 x 1 mm^3, resulting in approximately 335 million voxels. The sources contributing to the absolute uncertainty of the average dosimetry were *a*) antenna modeling; 0.1 dB (experimentally verified); *b*) deviation of incident field exposure with respect to the target field including transfer calibration, sensor linearity, feedback control, and reflections from furniture, 0.7 dB; and *c*) average anatomy, dielectric parameters, and discretizations. The variation as a function of weight, sex, and position was assessed separately by scaling the three phantoms in the range of our subjects (47-110 kg; head tissues were based on nonscaled phantoms) and by rotating the phantoms ±25° around their axis. Because of good uniformity of the field, we could neglect the effect of movement.

3.3.2.4 Questionnaires

The short Questionnaire on Current Disposition (QCD) (Müller and Basler 1993) measures subjective well-being within short test-retest intervals using six bipolar items (tense–calm, apprehensive–unperturbed, worried–unconcerned, anxious–relaxed, skeptical–trusting, uneasy–comfortable) and was applied before and after each experimental condition. Outcomes of the QCD comprise the difference between post and preexperimental scores (QCD_{diff}) as well as postexperimental scores (QCD_{post}). We used the modified Quality-of-Life Questionnaire (Zwamborn et al. 2003), henceforth referred to as the TNO-Q, as a reference questionnaire for comparison with the TNO study. The validated, original questionnaire had been developed to estimate “quality of life” during trials of an antihypertensive drug treatment (Bulpitt and Fletcher 1990) and was modified by Zwamborn et al. (2003) by using a selection of 23 items separated in five subscales (anxiety, somatic symptoms, inadequacy, depression, hostility). We applied a self-designed Questionnaire to include Other Factors (QOF) potentially related to well-being (sleep duration, quality of previous night, suffering from a cold, amount of alcohol and caffeine consumed and medication taken on the day of the experimental session, (pre)menstrual complaints, and stressful events). Moreover, subjects had to rate the perceived field strength of the same day’s exposure condition on a visual analogue scale

ranging from “not at all” (0) to “very strong” (100 mm). We applied the TNO-Q and the QOF after each experimental condition (Figure 10). Completion of all questionnaires took 5-15 min. One week before the training and 1 week after the last session, we applied a paper version of the Bern Questionnaire on Well-being (BQW) (Grob 1995). It measures well-being over a few weeks [39 items separated into two main scales (satisfaction, ill health)] and was used to assess whether participation per se had an influence on well-being, regardless of exposure.

3.3.2.5 Cognitive tasks

We investigated the effects of UMTS-like radiation on brain functioning with the SRT, CRT (Koivisto et al. 2000b; Preece et al. 1998; Preece et al. 1999), N-back Task (1-, 2-, 3-back, Koivisto et al. 2000a, see chapter 3.1.2.4 and 3.2.2.4) and the Visual Selective Attention Task (VSAT) adapted from Zwamborn et al. (2003). In the VSAT, a random combination of four letters and/or crosses in a square was presented. The targets were “U” and “F” appearing on the diagonal from upper left to lower right. Subjects had to press “J” when one or both targets appeared and “N” when no target was presented (see also the Appendix). All tasks were applied twice in fixed order (SRT, CRT, 1-, 2-, 3-back, VSAT). Completion of one series took 15-20 min.

3.3.2.6 Statistical Analysis

We used linear mixed models for statistical analyses questionnaires: STATA 9.0, StataCorp, College Station, TX, USA; cognitive tasks: SAS version 8.2; SAS Institute Inc., Cary, NC, USA). With respect to reaction times, we excluded individual outliers over all sessions according to a robust rejection estimation procedure (4 x median deviation, Hampel 1985). We transformed reaction times (1/reaction time), which are referred to as speed (1/s; correct responses only), and checked residuals for normal distribution. We performed stratified analyses for the sensitive and nonsensitive groups by using a random intercept model presuming an identical intraclass correlation for all subjects. The base model included the factor *Condition* (sham, 1 V/m, 10 V/m) and *Week* (1, 2, 3) to account for possible order effects. The model for cognitive data also contained *Session* (session 1, session 2) as a factor and corresponding interaction effects. We modeled condition as a continuous variable to test for a dose-response relationship and assessed

differences between groups with an overall model including the factor *Sensitivity* and a *Sensitivity x Condition* interaction. We evaluated the robustness of results by adjusting the model for potential confounding factors (Tables 10 and 12). We used the percentage of correct answers in the CRT, 1-, 2-, 3-back and VSAT as a measure of accuracy. Except for the 3-back data, residuals were not normally distributed, and differences were assessed using nonparametric Wilcoxon signed-rank tests. We performed comparisons of 1 V/m versus sham and 10 V/m versus sham for session 1, session 2, and the difference between the two sessions. The resulting *p*-values were adjusted for multiple testing (six tests) according to Bonferroni-Holm (Holm 1979). To generally control for multiple testing, we performed a multiple end point adjustment for the cognitive outcomes using the method proposed by Tukey et al. (1985). We analyzed the ability to perceive EMF by calculating Spearman rank correlations between perceived field intensity and true exposure status for each subject. We tested the number of positive and negative correlations using a sign test and used the same procedure to evaluate the association between perceived field intensity and well-being (QCD, TNO-Q).

3.3.3 Results

3.3.3.1 Questionnaires

Well-being as measured by the QCD and the TNO-Q was not affected by exposure (Table 10). With respect to the six items in the QCD and the five subscales of the TNO–Q, we found no significant exposure-response associations in any of the two groups. Regardless of the actual condition, sensitive subjects generally reported more health problems, particularly in the TNO-Q. Neither group showed a relationship between perceived field intensity and true exposure status (Table 11). Sensitive subjects indicated higher field strengths in all conditions ($p < 0.001$), even though score values were not associated with exposure levels. Seventeen of 31 sensitive subjects had a positive correlation between perceived and real field intensity, and 13 had a negative correlation (nonsensitive group, 22 and 27 of 57 subjects, respectively), which can be expected by chance (Table 11). Regardless of exposure condition, perceived field intensity was positively correlated with impaired wellbeing in 68% of sensitive (QCD_{diff}, $p = 0.043$) and 64% of nonsensitive ($p = 0.001$) subjects. Similar results were found with respect to the QCD_{post} and the TNO-Q (data not shown). In the BQW, comparison of scores 1-week before and after study participation showed no significant changes for

satisfaction and ill health in the sensitive group. In the nonsensitive group, the score for ill health was lower after the experiment ($p = 0.004$), but satisfaction remained unchanged.

Table 10: *Results of applied questionnaires (mean scores; SD in parenthesis; n = 33 sensitive and n = 84 nonsensitive subjects). Outcomes of the QCD (Short questionnaire on current disposition) comprise the difference between pre and post experimental scores (QCD_{Diff}) as well as post experimental scores (QCD_{post}). A difference score > 0 corresponds to a degradation in current well-being during the experiment. In the QCD_{post} and the TNO-Q (Quality-of-life questionnaire) higher scores refer to a lower well-being. Subjective field perception was measured by means of a 100 mm visual analogue scale ranging from "not at all" (0) to "very strong" (100 mm). We report only p-values of Condition (Cond) (for details, see section 3.3.2 "Materials and Methods").*

Outcome	Group	Sham Mean (SD)	1V/m Mean (SD)	10V/m Mean (SD)	Cond[a] p-value	Cond[b] p-value
QCD_{diff}	Sensitive	0.30 (0.83)	0.24 (0.99)	0.24 (0.95)	0.88	0.95
	Non-Sensitive	0.05 (0.73)	-0.04 (0.59)	0.02 (0.55)	0.93	0.95
QCD_{post}	Sensitive	2.57 (1.06)	2.65 (1.22)	2.61 (0.97)	0.97	0.96
	Non-Sensitive	2.19 (0.76)	2.05 (0.80)	2.13 (0.78)	0.97	0.89
TNO-Q	Sensitive	10.53 (9.51)	9.61 (8.96)	9.79 (8.38)	0.84	0.65
	Non-Sensitive	5.23 (5.09)	4.45 (4.92)	4.96 (5.08)	0.78	0.92
Field perception	Sensitive	26.0 (31.9)	31.2 (33.7)	29.4 (29.7)	0.89	0.67
	Non-Sensitive	12.9 (22.8)	5.7 (13.1)	12.2 (23.2)	0.24	0.33

[a] Adjusted for order; [b] Adjusted for order, age, sex, BMI, caffeine intake, medication, (pre-) menstrual complaints, sleep quality and suffering from a cold

Table 11: *Correlations between perceived electric field strength and real exposure condition (sham, 1 V/m, 10 V/m). Two sensitive and 27 nonsensitive subjects perceived no field in all three conditions and were omitted from the analysis.*

	Correlation between perceived and real field				
	N	**positive**	**negative**	**zero**	**p-value[a]**
All	88	39	40	9	1
Sensitive	31	17	13	1	0.58
Non-Sensitive	57	22	27	8	0.56

[a] Sign Test

3.3.3.2 Cognitive Tasks

In the course of the entire study, subjects got faster in all tasks ($p < 0.02$) except the SRT. In both groups and irrespective of condition, speed decreased significantly from session 1 to session 2 in both the SRT and CRT but increased in the 1-, 2-, 3-back and VSAT ($p < 0.0001$). In the following, only effects including C*ondition* or a C*ondition x Session* interaction are described. In both groups, we observed no condition induced effects on speed in the SRT, 1-, 2-, 3- back and VSAT. In the CRT, speed decreased in the sensitive group from session 1 to session 2 in the sham and 1 V/m condition (~ 20 ms), but not in the 10 V/m condition (*Condition* x *Session*, $p = 0.007$; Table 12). In contrast, we observed a decrease in speed between sessions irrespective of exposure condition in the nonsensitive group ($p = 0.254$; Table 12). A mixed-model analysis of variance including the factor sensitivity (sensitive, nonsensitive) corroborated the observed differences between groups with respect to exposure (*Condition* x *Sensitivity*, $p = 0.005$). Accuracy was not affected by exposure in a dose-response manner in any of the cognitive tasks except the 1-back task in the nonsensitive group, where it decreased from 98.2% (sham) to 97.3% (10 V/m; $p = 0.046$) in session 1.

Table 12: *Results of cognitive performance. Mean speed (1/Reaction time [1/s]; SD in parenthesis; n = 33 sensitive and n = 84 nonsensitive subjects) in the two sessions (first and second half of exposure) in the SRT (Simple reaction time task), CRT (Two choice reaction time task), N-back task (1-, 2-, 3-back) and VSAT (Visual selective attention time task). We report only p-values of Condition (Cond) and of the interaction Condition*Session (for details, see section 3.3.2 "Materials and Methods"). Statistical analysis is based on data of all subjects. Because of a missing session in some subjects, mean values are based on subjects who completed both sessions in each condition (n = at least 32 sensitive and at n = at least 77 nonsensitive subjects).*

Outcome	Group	Session	Sham mean (SD)	1V/m mean (SD)	10V/m mean (SD)	Cond[a,c] p-value	Cond*Session[a,c] p-value	Cond[b,c] p-value	Cond*Session[b,c] p-value
SRT	Sensitives	1	3.86 (0.52)	3.78 (0.44)	3.84 (0.48)	0.09	0.27	0.07	0.27
		2	3.73 (0.56)	3.65 (0.43)	3.78 (0.47)				
	Non-Sensitives	1	3.85 (0.37)	3.85 (0.38)	3.84 (0.43)	0.59	0.51	0.37	0.50
		2	3.70 (0.44)	3.70 (0.49)	3.68 (0.41)				
CRT	Sensitives	1	2.37 (0.28)	2.33 (0.25)	2.33 (0.28)	0.03	0.01	0.02	0.01
		2	2.25 (0.30)	2.20 (0.27)	2.31 (0.22)				
	Non-Sensitives	1	2.27 (0.26)	2.27 (0.27)	2.24 (0.25)	0.13	0.25	0.08	0.24
		2	2.22 (0.27)	2.21 (0.27)	2.21 (0.25)				
1-Back	Sensitives	1	2.15 (0.56)	2.12 (0.55)	2.13 (0.55)	0.90	0.67	0.93	0.67
		2	2.27 (0.57)	2.29 (0.54)	2.29 (0.49)				
	Non-Sensitives	1	2.12 (0.44)	2.12 (0.48)	2.10 (0.42)	0.57	0.97	0.46	0.98
		2	2.25 (0.44)	2.28 (0.48)	2.24 (0.43)				

Outcome	Group	Session	Sham mean (SD)	1V/m mean (SD)	10V/m mean (SD)	Cond[a,c] p-value	Cond*Session[a,c] p-value	Cond[b,c] p-value	Cond*Session[b,c] p-value
2-Back	Sensitives	1	1.59 (0.46)	1.53 (0.44)	1.53 (0.35)	0.61	0.44	0.50	0.43
		2	1.70 (0.49)	1.71 (0.53)	1.71 (0.47)				
	Non-Sensitives	1	1.63 (0.39)	1.58 (0.39)	1.60 (0.38)	0.44	0.52	0.37	0.52
		2	1.74 (0.42)	1.74 (0.43)	1.72 (0.39)				
3-Back	Sensitives	1	1.48 (0.40)	1.48 (0.46)	1.48 (0.39)	0.57	0.52	0.39	0.51
		2	1.56 (0.42)	1.60 (0.51)	1.54 (0.37)				
	Non-Sensitives	1	1.56 (0.44)	1.57 (0.51)	1.51 (0.36)	0.59	0.11	0.64	0.11
		2	1.70 (0.55)	1.64 (0.50)	1.70 (0.49)				
VSAT	Sensitives	1	1.74 (0.33)	1.72 (0.31)	1.75 (0.31)	0.28	0.94	0.22	0.94
		2	1.85 (0.29)	1.85 (0.31)	1.87 (0.28)				
	Non-Sensitives	1	1.69 (0.34)	1.69 (0.33)	1.68 (0.29)	0.64	0.70	0.50	0.71
		2	1.78 (0.32)	1.83 (0.36)	1.79 (0.31)				

[a] Adjusted for order; [b] Adjusted for order, age, sex, BMI, caffeine intake, medication, (pre-) menstrual complaints, sleep quality and suffering from a cold

Adjusting the model for potential confounding factors (Tables 10 and 12) or performing the analyses with only the 1:1 matched subjects did not alter the results. After multiple end point adjustment (α = 0.05; number of tests = 44; overall correlation among cognitive outcomes = 0.39), however, all reported *p*-values exceeded the significance level of $p = 0.0051$ (Tukey et al. 1985).

3.3.3.3 Dosimetry

Penetration depth was low, and highest SAR values occurred predominantly at the illuminated side close to the skin (Table 13, Figure 12).

Table 13: *Averaged SAR values for whole body and brain and peak spatial averaged SAR for whole body, brain, skin, and muscle for an E-field strength of 1 V/m. Data are, for an E-field strength of 1 V/m, averaged SAR values ± SD of variations and the absolute uncertainty [95% confidence interval (CI)] for whole body and brain, and peak spatial averaged SAR for whole body, brain, skin and muscle (1 and 10 g) of an average male (80 kg). To obtain SAR values at a field strength of 10 V/m, SAR values in the table have to be multiplied by 100.*

Tissue	**SAR [average ± SD (µW/kg)]**	**Uncertainty [95% CI (%)])**
Whole body	6.2 (1.8)	41
10 g (peak spatial)	150 (49)	39
1 g (peak spatial)	320 (130)	41
Brain	11 (2.4)	48
10 g (peak spatial)	45 (13)	45
1 g (peak spatial)	73 (16)	44
Skin		
10 g (peak spatial)	230 (48)	50
1 g (peak spatial)	380 (76)	39
Muscle		
10 g (peak spatial)	120 (31)	48
1 g (peak spatial)	190 (62)	39

Whole-body average absorption was 6.2±1.8 and 620±180 µW/kg for 1 V/m and 10 V/m, respectively, with an absolute uncertainty of 41% (Table 13). Peak spatial SAR (averaged over 10 g) was 45±13 and 4,500±1,300 µW/kg, respectively, for brain tissue. At 10 V/m, all values were at least 100 times below recommended safety limits (ICNIRP 1998). Compared with use of a mobile phone at the ear or exposure levels used in other studies, the peak spatial SAR of the brain was > 100 times lower at 10 V/m in our study. SAR values for head tissues and left-right differences are shown in Table 14. The SAR values are strongly dependent on the incidence angle and the polarization of the field that were fixed in our study. Variation of incidence angle and polarization at the same field strength will lead to considerable changes of the SAR values in different parts of the body.

Table 14: *Ratios of averaged SAR values between various organs or tissue and whole body and between left and right sides. Data are ratios, for an average male (80 kg), between organ or tissue averaged SAR values and the whole-body averaged SAR value (6.2 µW/kg at 1 V/m) for regions of the brain, ear, eye, and throat and the ratio between the averaged SAR values of the left and right sides.*

Organ/Tissue	Ratio organ or Tissue / whole body	Ratio left / right
Grey matter (left hemisphere)	3.5	2.9
White matter (left hemisphere)	2.0	2.6
Cerebellum	0.52	-
Hippocampus (left hemisphere)	0.84	1.6
Hypothalamus (left hemisphere).	0.52	1.9
Thalamus (left hemisphere)	0.64	0.81
Parotid gland	4.6	-
Ear pinna (left)	17	18
Eye ball (left)	5.6	8.8

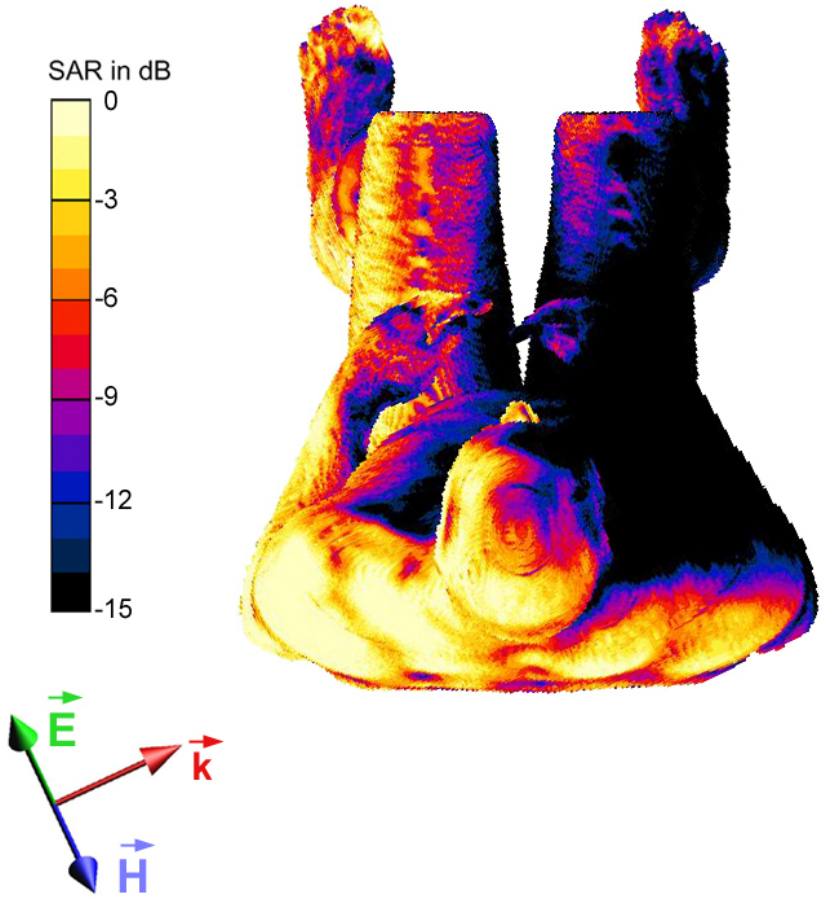

Figure 12: *SAR distribution on the surface of a male (80 kg) in a sitting position (top view): 0 dB corresponds to 0.05 W/kg for an E-field strength of 1 V/m, The orientation of the E-field ($\vec{E}$), the magnetic field ($\vec{H}$), and the propagation direction ($\vec{k}$) of the EMF are indicated.*

3.3.4 Discussion

In contrast to our hypothesis, well-being as assessed by the QCD and TNO-Q questionnaires was not affected by UMTS radiation, either in the 1 V/m or in the 10 V/m condition. Even though sensitive subjects generally reported more health problems, we found no difference overall between the two groups with respect to the applied field conditions. Similarly, cognitive performance was not affected except for two separate and marginal effects in the 10 V/m condition. In the CRT we could not observe a slight decrease in speed across sessions in sensitive subjects as observed in the 0 V/m and the 1 V/m condition, and in the 1-back task accuracy was reduced in nonsensitive subjects compared to the sham condition. Cognitive tasks with moderate to high

workload frequently have been used as a tool to assess RF EMF effects on brain physiology by measuring simple motor responses requiring selective attention and higher cognitive functions such as working memory (e.g., Krause et al. 2000b). Except for the VSAT, which was taken from the TNO battery of cognitive tasks for follow-up reasons, we chose the SRT, CRT, and N-back on the basis of recently published work attempting to assess EMF-induced changes with respect to brain physiology (Koivisto et al. 2000a; 2000b; Preece et al. 1999). However, the described effects showed no consistent picture and could not be replicated (Haarala et al. 2003b; Preece et al. 2005). In general, exposure in these studies was poorly defined, and the inconsistencies in cognitive outcome may be due to differences in the design, blinding, study population, and sample size, thus preventing a comparison of the results. Alternatively, cognitive tasks used so far may not be sensitive enough to reliably measure potential RF EMF effects on brain functioning, leading to a masking of existing effects or resulting in significant effects of tests that stochastically respond to RF EMF. Moreover, statistical analysis of several tests increases the risk of false-positive findings. In the present study, speed was affected in the sensitive group in one of six cognitive tasks and accuracy in the nonsensitive group in one of five tasks. Although we cannot exclude an actual *Condition x Session* interaction in the CRT in sensitive subjects and, similarly, a condition effect in the 1-back task in nonsensitive subjects, the findings seem to be coincidental because they did not reach significance after multiple end point adjustment. Both the sensitive and the nonsensitive groups were unable to identify the applied fields better than expected by chance. Because we investigated only three conditions per subject, the likelihood of correct field rating by chance was relatively high. The observed distribution of 39 individuals with a positive correlation between the applied and estimated exposure conditions and 40 individuals with a negative correlation was likely to be expected by chance. Nevertheless, we cannot exclude that among these subjects a minority was actually able to perceive the applied exposure. The identification of such individuals has failed in several provocation studies so far (reviewed by Rubin et al. 2005) and would require a multiple testing approach to reduce the likelihood of a correct rating by chance. Perceived field strength correlated with an impairment of current well-being in both groups irrespective of exposure condition. Also, sensitive subjects rated perceived field strengths higher than did nonsensitive subjects, yet ratings in both groups were not better than expected by chance and not associated with exposure levels. This indicates that sensitive subjects overestimate their ability to better perceive

RF EMF than does the general public (Leitgeb and Schröttner 2003). Our results differ with respect to both well-being and cognitive performance from the results reported by Zwamborn et al. (2003). The TNO-Q is an adapted and not validated version of the original questionnaire (Bulpitt and Fletcher 1990) and was not designed for short retest intervals. Our findings were corroborated by the results of the QCD, a standardized questionnaire that more reliably measures changes in well-being over short test-retest intervals (Müller and Basler 1993). Contrary to the TNO study, we found no significant effect on speed in the VSAT. It was, however, the only task applied in both studies; all other cognitive tasks were distinct. Zwamborn et al. (2003) found other effects with respect to cognitive tasks and exposure conditions (GSM and UMTS), and we also report an effect on speed in one of six tasks and an effect on accuracy in one of five tasks used. No clear picture, therefore, emerges across the two studies showing reproducible effects of exposure condition or cognitive task. A number of other factors may contribute more generally to the discrepancies between the TNO study and our study. Sample sizes differ substantially (sensitive subjects, 24 vs. 33; nonsensitive subjects, 24 vs. 84). Our reference group was frequency matched to the sensitive group, and a subgroup was 1:1 matched with respect to sex, age, residential area, and BMI. In the TNO study, all conditions in a particular subject were carried out on a single day, whereas we investigated the subjects at the same time of day in weekly intervals to rule out possible circadian and carryover effects. We further controlled circadian influences by a uniform distribution of experimental sessions across the time of day. Carryover effects may lead to an accumulation of RF EMF radiation over time, thus falsifying potential effects of discrete conditions. Furthermore, inclusion of an additional E-field strength of 10 V/m is likely to have contributed to a more reliable assessment of RF EMF effects. Technical improvements necessitated the modification of the exposure setup used in the TNO study to achieve a more uniform and reproducible base station-like exposure. Although the signal (carrier frequency and modulation) and the angle of incidence were identical, the spatial incident field distribution was less uniform in the TNO study, where a narrow exposure beam of only 5° width was used, resulting in a larger variation because of differences in height and position of the subjects. In addition, the whole-body exposure conditions applied in this study correspond better to a base-station exposure scenario. However, exposure of head tissues was equivalent in both studies, even though we had a smaller intersubject variability. Further insights regarding the discrepancies between the present and the Dutch study might be gained from other

follow-up studies under way in Denmark, the United Kingdom, and Japan, which are also investigating the effect of UMTS base station-like radiation on well-being and cognitive function (Andersen J, Challis L, Watanabe S, personal communications). In summary, we found no causal relationship between RF EMF and a decrease in well-being or adverse health effects under the given exposure conditions but cannot exclude an effect of UMTS-like EMF on brain functioning. The described effects were weak and not consistent in the two groups of sensitive and nonsensitive subjects. Regarding the implications for public health because of widespread exposure in the living environment, no conclusions about long-term effects of UMTS base station-like EMF can be drawn from the present study, since only a short-term exposure was applied.[◊]

[◊] Coinvestigators of this study were:

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4 CONCLUDING REMARKS

In this thesis the influence of RF EMF exposure on brain physiology and subjective well-being was investigated. Two studies examined the effects of mobile phone RF EMF exposure on the waking and the sleep EEG and cognitive performance in 24 and 15 healthy young males, respectively. In a third study we assessed base station-like RF EMF exposure on well-being and cognitive performance in 33 self-reported electrosensitive and 84 self-reported non-electrosensitive male and female individuals. The measures under investigation included polygraphic recordings (EEG, EOG, EMG) during waking and sleep, speed and accuracy of performance in several cognitive tasks and well-being ratings by means of questionnaires. Consistent with previous studies we showed 1) an increase in alpha activity in the waking EEG, and 2) increased spectral power in the spindle-frequency range in stage 2 non-REM sleep after exposure, and 3) variable findings with respect to cognitive performance during exposure. The absence of impaired well-being during UMTS base-station exposure (chapter 3.3) contrasts with the results reported previously (Zwamborn et al. 2003).

At present, evidence suggests that brief exposure to RF EMF can have slight effects upon electrophysiological parameters and cognition in humans. Nevertheless, studies so far yield contradictory and partly non-reproducible findings. The results are difficult to compare. In general, various factors should be taken into account which may increase the variance within and across studies, i.e., differences with respect to the number of subjects and the study population (e.g., age, gender, special class of patients), the experimental design (e.g., blinding, time interval between active and inactive exposure) or the exposure characteristics (intensity, frequency, waveform, exposure duration, side of exposure, distance to source) but also time of testing (during vs. following exposure) or the implementation of a variety of different tasks which are generally not comparable. The literature summarized in this thesis (chapter 2) provides a fairly representative overview on electrophysiological and cognitive effects in humans. Yet, mainly due to the methodological issues listed above, one should be cautious when comparing the results. Whereas some experiments, for example, included a highly controlled exposure setup (e.g., Borbély et al. 1999; Huber et al. 2000; 2002; 2003; 2005), the majority has used actual or simulated mobile telephones to expose subjects to RF EMF in their studies (e.g., Croft et al. 2002; Curcio et al. 2004; D'Costa et al. 2003; Eliyahu et al. 2006;

Haarala et al. 2003a; 2004; Hamblin et al. 2004; Hietanen et al. 2000; Jech et al. 2001; Keetley et al. 2006; Lee et al. 2003; Loughran et al. 2005; Preece et al. 2005; Smythe and Costall 2003). Relevant variations exist especially with respect to the positioning of the phone. This variability is even increased in experiments in which the phone is not fixed in a predefined position, but has to be held with one hand to one ear by the study participants during exposure (e.g., Besset et al. 2005; Edelstyn and Oldershaw 2002; Smythe and Costall 2003; Yuasa et al. 2006). Various field conditions are described in various manners. Information on power (W), power density (W/m^2) or specific absorption rate (W/kg) is very difficult to compare, if at all. The SAR is an important measure as it specifies the amount of energy absorbed by the underlying biological tissue per units of time and mass (compare chapter 1.7.3), yet, it is rarely mentioned in the publications. In addition, it is not possible to calculate the specific absorption rate on the basis of e.g., the power density. In principle, one can request the max. SAR for a GSM mobile phone from the manufacturer (~ 0.2-1.5 W/kg). These SAR values apply in case the mobile phone is in direct contact to the head. With increasing distance, though, these estimates cannot be applied, but instead sophisticated dosimetry (computer simulation, phantom measurements) is needed.

In the following, a critical evaluation of the literature summarized in chapter 2 is provided. After focusing on electrophysiological recordings, the chapter continues with a discussion of the different findings on cognitive performance. A general conclusion completes this chapter.

4.1 Electrophysiological Recordings

Several variables complicate the comparison of the results in the EEG literature. First of all, in seven out of eight waking EEG studies summarized in this thesis EOG and/or EMG recordings were not specified in the papers (Croft et al. 2002; D'Costa et al. 2003; Hietanen et al. 2000; Hinrikus et al. 2004; Reiser et al. 1995; Röschke and Mann 1997; von Klitzing 1995). A similar picture emerges regarding ERP recordings (e.g., Croft et al. 2002; Eulitz et al. 1998; Freude et al. 1998; 2000; Krause et al. 2000a; 2000b) which in particular raises concern regarding the removal of artifacts and subsequent statistical data analysis in these studies. Besides, only a single experiment assessed changes in the waking EEG with eyes open (Croft et al. 2002), all the others with eyes closed (D'Costa et al. 2003; Hietanen et al. 2000; Hinrikus et al. 2004; Röschke and Mann

1997; von Klitzing 1995). Two of the studies did not specify the recording condition at all (Curcio et al. 2005; Reiser et al. 1995). In general, awake and sleep EEG recordings were obtained during exposure (Borbély et al. 1999; Croft et al. 2002; D'Costa et al. 2003; Hietanen et al. 2000; Mann and Röschke 1996; Röschke and Mann 1997; Wagner et al. 1998; 2000), after exposure (Huber et al. 2000; 2002; Loughran et al. 2005; Pasche et al. 1996), or both during and after exposure (Curcio et al. 2005; Hinrikus et al. 2004; Reiser et al. 1995; von Klitzing 1995). In ten studies, ERP recordings were obtained during exposure (Croft et al. 2002; Eulitz et al. 1998; Freude et al. 1998; 2000; Hamblin et al. 2004; Hinrichs and Heinze 2004; Jech et al. 2001; Krause et al. 2000a; 2000b; 2004) and in one before and after exposure (Yuasa et al. 2006). Therefore, in a large number of cases, RF EMF exposure and electrophysiological measurements were applied simultaneously. Only a few studies, however, specified a proper shielding of the recordings system and the amplifier during RF EMF exposure (e.g., Borbély et al. 1999; Mann and Röschke 1996). Therefore, in a great proportion of studies, interference between RF EMF and the recording equipment cannot be excluded. In this context it is also important to stress the orientation of the electrode-wires (horizontally/vertically with respect to the antenna) as it may influence the distribution of the field during exposure; this aspect is practically never mentioned in the literature. The results may hence reflect not only treatment related changes, but also measurement artifacts.

A high variability also exists with respect to the exposure duration. Apart from Eulitz et al. (1998) and Freude et al. (2000) who do not explicitly provide this information in their papers, it ranges from 3.5 min to 45 min in studies on waking (Curcio et al. 2005; Röschke and Mann 1997), 20 min to 2 consecutive nights of 8 h in studies on sleep (Pasche et al. 1996; Wagner et al. 2000) and 8 min to 60 min for ERP recordings (Freude et al. 1998; Hamblin et al. 2004). Due to vigilance changes in the course of the experiment, an increase in exposure and recording duration may generally increase the variability within and across subjects (Croft et al. 2002). For example, alpha activity is sensitive to alterations in attention and alertness in waking (e.g., Klimesch 1999; Niedermeyer 2005). Depending on the duration of the experiment and the recording conditions (e.g., eyes closed, eyes open), corresponding changes in alertness may therefore affect alpha activity. This might on the one hand mask a mobile-phone related alpha change (Croft et al. 2002), but on the other hand also potentially increase the likelihood of a chance finding. Moreover, possible variations exist with respect to the EEG setup (e.g., number and placement of electrodes, appropriate filter settings) and

analysis techniques in several studies. Therefore, it is generally difficult to draw a final and universal valid conclusion regarding the affected frequencies or frequency bands, amplitudes or topographical changes.

According to Rosenthal (Rosenthal 1968), double-blind experiments are necessary to prevent a possible systematic bias in scientific research. Despite the knowledge that intrinsic expectations about the experimental conditions can influence the study outcome by interactions between the experimenter and the subjects of the experiment ("Self-fulfilling prophecy", overviewed in Rosenthal 1968), several studies reviewed in chapter 2 were performed single-blind or even not blinded at all. Specifically, only one out of eight studies on the waking EEG was performed under double-blind conditions (Curcio et al. 2005). Seven studies on ERP were conducted with a single-blind design (Croft et al. 2002; Eulitz et al. 1998; Freude et al. 1998; 2000; Hamblin et al. 2004; Krause et al. 2000a; 2000b), three with a double-blind design (Hinrichs and Heinze 2004; Jech et al. 2001; Krause et al. 2004) and one study without either blinding the experimenters or the subjects (Yuasa et al. 2006). In contrast, the majority of studies on the sleep EEG (six out of eight) were performed double-blind (Borbély et al. 1999; Huber et al. 2000; 2002; Loughran et al. 2005; Pasche et al. 1996; Wagner et al. 1998).

4.2 Cognitive Performance

Besides the difficulties mentioned for electrophysiological recordings, several aspects complicate the classification of the results reported on cognitive performance so far. Whereas initially mainly "positive" findings, i.e., an improvement of cognitive performance was reported in response to RF EMF exposure (e.g., Koivisto et al. 2000a; 2000b; Preece et al. 1999; Smythe and Costall 2003), more and more "negative" results are aggregating now as research proceeds (e.g., Hamblin et al. 2004; Keetley et al. 2006; Lass et al. 2002; Preece et al. 2005). Out of the 17 studies summarized in chapter 2.5 and six studies summarized in chapter 2.3, including various cognitive tasks, six studies revealed an increase (Curcio et al. 2004; Jech et al. 2001; Koivisto et al. 2000a; 2000b; Lee et al. 2003; Preece et al. 1999) and three studies a decrease in performance speed (Eliyahu et al. 2006; Hamblin et al. 2004; Keetley et al. 2006). Error scores were reduced and elevated in three experiments, respectively (Krause et al. 2004; Lass et al. 2002; Smythe and Costall 2003). One group reported increased memory capacity (Edelstyn and Oldershaw 2002), another one decreased retrieval efficiency in one task (Keetley et al. 2006). Ten studies observed no changes on

cognitive performance at all (Besset et al. 2005; Freude et al. 2000; Haarala et al. 2003b; 2004; 2005; Hinrichs and Heinze 2004; Krause et al. 2000b; Preece et al. 2005; Russo et al. 2006; Schmid et al. 2005). As a result, despite a growing amount of literature, the outcomes become more and more inconsistent. The different findings might partly be due to differences in the experimental design, the exposure setup and the conditions. They might, however, be also due to the lack of a validated tool, which reliably assesses cognitive performance changes caused by RF EMF exposure.

Generally, several different tasks addressing different modalities with a varying degree of difficulty are applied in one single study (e.g., Keetley et al. 2006; Koivisto et al. 2000b). Yet so far, only selective tasks, but not a whole test battery yielded significant results. Most importantly, the significances do not seem to depend on a specific type of task (e.g., attention, memory) or follow any rule. This non-specificity (e.g., an increase in speed in one task and a decrease in another task) is difficult to interpret. As discussed in chapter 3.3.4, it is most likely that either the tasks are not sensitive enough to reveal an induced effect or that significant performance changes might have simply occurred by chance as most authors did not adjust their *p*-values for multiple testing. This assumption gains further support by the lack of reproducibility of previous results under improved methodology as seen in several follow-up studies (e.g., Haarala et al. 2003b; 2004; Preece et al. 2005). As already referred to previously, changes in the exposure setup might be responsible for the lack of reproducibility in some cases. For example, trying to validate the results reported by Koivisto et al. (2000a), Haarala et al. (2004) used both a higher averaged SAR_{10g} and peak SAR in their replication study. Moreover, the peak SAR was closer to the cortex (Haarala et al. 2004).

The blinding of both experimenter and participants is important to gain objective data. Whereas ten studies were performed with a single-blind design (Edelstyn and Oldershaw 2002; Eliyahu et al. 2006; Freude et al. 2000; Hamblin et al. 2004; Koivisto et al. 2000a; 2000b; Krause et al. 2000b; Lass et al. 2002; Lee et al. 2003; Smythe and Costall 2003) a slightly larger number of experiments used double-blind conditions to assess performance changes due to RF EMF (13 studies, Besset et al. 2005; Curcio et al. 2004; Haarala et al. 2003b; 2004; 2005; Hinrichs and Heinze 20004; Jech et al. 2001; Keetley et al. 2006; Krause et al. 2004; Preece et al. 1999; 2005; Russo et al. 2006; Schmid et al. 2005). In addition to the blinding conditions, the duration of exposure and recordings per se might influence alertness or vigilance and therefore also performance parameters.

Especially very simple or very difficult tasks might induce fatigue and/or motivational loss in subjects and thus accelerate these alterations. Based on the literature summarized in chapter 2.5 and 2.3, the study of Bessett et al. (2005) constitutes an exception as this study assessed the effects before, during and after long-term RF EMF exposure on cognitive performance (2 h per day, 5 days per week, 4 weeks). To date, durations of short term exposure vary from 10-20 min (Lass et al. 2002; Smythe and Costall 2003) to 120 min (Eliyahu et al. 2006). Schmid et al. (2005) did not specify the exact exposure duration. In 20 cases performance was assessed during exposure (Curcio et al. 2004; Eliyahu et al. 2006; Freude et al. 2000; Haarala et al. 2003b; 2004; 2005; Hamblin et al. 2004; Hinrichs and Heinze 2004; Jech et al. 2001; Koivisto et al. 2000a; 2000b; Krause et al. 2000b; 2004; Lass et al. 2002; Lee et al. 2003; Preece et al. 1999; 2005; Russo et al. 2006; Schmid et al. 2005; Smythe and Costall 2003), once before and during exposure (Keetley et al. 2006), once before and after exposure (Edelstyn and Oldershaw 2002) and once only after exposure (Curcio et al. 2004). As a certain exposure time might be needed to induce an observable effect (see also discussion in chapter 3.1.4), it might be very difficult to find the right balance between the appropriate exposure duration and the exact timing (beginning/end) and duration of the applied cognitive tasks. Moreover, the sequence of the task might be an important factor. If really a certain “preload” of RF EMF exposure is needed to measure changes in cognitive performance, tasks which are applied at the very beginning of a session will never show significant changes, however, not because of the task itself but simply because of the point in time where the task is introduced within the experiment. It would be interesting to see if the reported effects published so far did not appear in the first tasks but rather in tasks applied in the course of the experiments. Unfortunately, the sequence of tasks is rarely mentioned in the literature.

In general, the following types of different cognitive tasks have been applied in EMF research: simple and complex motor tasks (Besset et al. 2005; Curcio et al. 2004; Haarala et al. 2003b; 2005; Keetley et al. 2006; Koivisto et al. 2000b; Preece et al. 1999; 2005; Russo et al. 2006), attention, vigilance and (working) memory tasks (Besset et al. 2005; Curcio et al. 2004; Edelstyn and Oldershaw 2002; Haarala et al. 2003b; 2004; Keetley et al. 2006; Koivisto et al. 2000a; 2000b; Lass et al. 2002; Lee et al. 2003; Preece et al. 1999; 2005; Russo et al. 2006; Smythe and Costall 2003) and visual or auditory oddball tasks (Hamblin et al. 2004; Jech et al. 2001). Tasks, however, differ with

respect to stimulus presentation and the type of response required for the respective stimulus. In general, simple motor responses (e.g., pressing a button by one finger) constitute the most often recorded parameter. A high variability exists, however, with respect to the hand or the fingers used to respond to a specific stimulus (e.g., Keetley et al. 2006; Koivisto et al. 2000a; 2000b; Preece et al. 1999), if specified at all in the respective papers. Responses were recorded by pressing corresponding response buttons on a keyboard (e.g., Haarala et al. 2004) or on a special response box (e.g., Preece et al. 1999). Despite motor responses, also verbal answers have been assessed (e.g., Haarala et al. 2004), making the comparison of even the same task more difficult as the answer modalities are not comparable (e.g., Haarala et al. 2004; Koivisto et al. 2000b).

4.3 General Conclusions

The results on waking and sleep EEG presented in study I (chapter 3.1) and study II (chapter 3.2) in this thesis are well in line with the literature (see chapter 2.1 and 2.2) and provide further support that RF EMF can influence brain physiology. Nevertheless, various different parameters may have an influence on the study outcomes in RF EMF research which complicates the direct comparison of the results and the drawing of a final conclusion. Several recent studies reported that exposure around 900 MHz had an effect on awake and sleep EEG power spectra (e.g., Borbély et al. 1999; D'Costa et al. 2003; Hietanen et al. 2000; Huber et al. 2000; 2002; Loughran et al. 2005). Alpha and sleep spindle activity seem to be the two most consistently affected variables in EMF research on waking and non-REM sleep, respectively (e.g., Borbély et al. 1999; Curcio et al. 2005; D'Costa et al. 2003; Huber et al. 2000; 2002; 2003; Loughran et al. 2005). Unlike EEG power spectra, previous observations on changes in sleep architecture (Mann and Röschke 1996; Pasche et al. 1996), which have been retested partly under stronger methodological control, could not be corroborated (e.g., Wagner et al. 1998; 2000). Huber et al. (2002; 2003; 2005) could not confirm the reduced waking after sleep onset found by Borbély et al. (1999), though it is important to note that the time point of exposure was different in these studies (exposure during sleep (Borbély et al. 1999) vs. exposure prior to sleep (Huber et al. 2002; 2003; 2005)). Likewise, we did not observe any effects of RF EMF exposure prior to sleep on conventional sleep parameters such as sleep latency or total sleep time, neither after exposure at a SAR_{10g} of 0.2 W/kg nor at

a SAR_{10g} of 5 W/kg (see chapter 3.2). Therefore, our carefully controlled studies yielded highly reproducible results.

A general conclusion regarding RF EMF induced cognitive performance changes is complicated as we found 1) reduced reaction speed in the 1- and 2-back task and increased accuracy in the 3-back task in study I (see chapter 3.1), 2) a trend of decelerating response times with increasing field intensity in study II (see chapter 3.2), and 3) no effects in study III after adjusting for multiple endpoints (see chapter 3.3). These results stand in contrast to what had been previously reported (Koivisto et al. 2000a; 2000b; Preece et al. 1999; Zwamborn et al. 2003). The SRT, CRT, N-back and the VSAT in our studies were chosen on the basis of previously published work (Koivisto et al. 2000a; 2000b; Preece et al. 1999; Zwamborn et al. 2003). As already mentioned, no specific task exists to reliably assess RF EMF induced changes on cognitive performance. We tried to follow-up on tasks previously used in RF EMF research as different outcomes of different tasks are generally not comparable. Moreover, we intended to obtain more information on the task sensitivities and applied them under highly controlled conditions. On purpose we chose tasks with a varying degree of difficulty as it may well be that not the task per se but the difficulty of the task is the important variable in measuring an effect. Thus, a task might be too easy or too difficult and therefore mask a RF EMF induced performance change. In all our studies we controlled for possible learning effects by applying a training session one week prior to the first experimental appointment. Only right-handers were recruited as participants and responses were always obtained with the right index and middle-finger on a standardized response box. We applied each cognitive test twice in exactly the same order: once during the first half of the exposure session and once during the second half of the exposure session. This was to control that the sequence of the tasks itself might not mask a possible effect (see chapter 4.2). Furthermore, the sequence of stimuli in each cognitive task and the inter stimulus intervals were chosen at random therefore simulating parallel test forms.

Regarding well-being, study III (see chapter 3.3) was performed as a follow-up experiment on Zwamborn et al. (2003). Under improved methodological conditions we could not confirm the reported reduction in well-being after UMTS base station-like exposure in electrosensitive and non-electrosensitive subjects. By now, no further well-controlled laboratory studies exist regarding the impact of RF EMF exposure at base station intensities on well-being. The possible reasons for the contradictory results of

Zwamborn et al. (2003) and ourselves have been discussed in chapter 3.3.4. Yet, it is important to stress that both studies assessed changes in well-being after short-term base station-like RF EMF exposure. The continuously increasing number of mobile phone users strengthens the need to investigate especially long-term effects of RF EMF of mobile communication systems on well-being and brain functioning. Moreover, it would be necessary to include children in future studies. In humans, the studies performed to date mainly assessed the responses to RF EMF exposure in young and middle-aged male and female subjects (~ 20-60 years). Children might represent a specifically sensitive subgroup as their brain is not yet completely mature at an early age. Therefore, it might be possible that children react differently to RF EMF exposure. In line with this, two recent studies in 10-14 year-old boys (Haarala et al. 2005; Preece et al. 2005) could not corroborate influences on cognitive performance found in adults (Koivisto et al. 2000a; 2000b; Preece et al. 1999).

The reviewed publications as well as our own research studies presented in this thesis indicate that short-term RF EMF exposure primarily at handset-intensities can induce biological changes. By definition, biological effects constitute a measurable reaction to a stimulus or an environmental change, yet, these changes may not necessarily involve negative health consequences. Indeed, little conclusive proof exists that EMF, at low exposure levels, reduce well-being or are even harmful. In this respect, it is important to note that most studies did not focus on this specific problem. At present, no underlying biological mechanism has been identified with respect to EMF mediated effects. Therefore, it is difficult to create a standardized protocol with fixed exposure conditions, intensities and durations in order to increase the validity and reliability of the data. Furthermore, in actual non-laboratory conditions electromagnetic fields are never encountered in isolation from other radiation sources, which in combination may modify the observed effects (Croft et al. 2002). This thesis provides indications that pulse modulation might play an important role in mediating the effects (compare chapter 3.1). It is important to determine this aspect in the future. Only then the relevance of the reported effects can be judged and a risk assessment can be established. Until then, precautionary measures should be taken, including the use of hands-free devices and restricting usage especially in children (World Health Organization 2000).

5 REFERENCES

Aalto S, Haarala C, Brück A, Sipilä H, Hämäläinen H, Rinne JO. 2006. Mobile phone affects cerebral blood flow in humans. J Cereb Blood Flow Metab 26:885-890.

Achermann P, Borbély AA. 1997. Low-frequency (< 1 Hz) oscillations in the human sleep EEG. Neuroscience 81:213-222.

Achermann P, Borbély AA. 1998a. Temporal evolution of coherence and power in the human sleep electroencephalogram. J Sleep Res 7:36-41.

Achermann P, Borbély AA. 1998b. Coherence analysis of the human sleep electroencephalogram. Neuroscience 85:1195-1208.

Adair ER, Black DR. 2003. Thermoregulatory responses to RF energy absorption. Bioelectromagnetics (Suppl.):S17-S38.

Aeschbach D, Borbély AA. 1993. All-night dynamics of the human sleep EEG. J Sleep Res 2:70-81.

Aeschbach D, Cajochen C, Tobler I, Dijk DJ, Borbély AA. 1994a. Sleep in a sitting position: Effect of triazolam on sleep stages and EEG power spectra. Psychopharmacology 114:209-214.

Aeschbach D, Dijk DJ, Trachsel L, Brunner DP, Borbély AA. 1994b. Dynamics of slow-wave activity and spindle frequency activity in the human sleep EEG: Effect of midazolam and zopiclone. Neuropsychopharmacology 11:237-244.

Aeschbach D, Dijk DJ, Borbély AA. 1997. Dynamics of EEG spindle frequency activity during extended sleep in humans: Relationship to slow-wave activity and time of day. Brain Res 748:131-136.

Altenmüller EO, Münte TF, Gerloff C. 2005. Neurocognitive functions and the EEG. In: Electroencephalography: Basic principles, clinical applications, and related fields (Niedermeyer E, Lopes da Silva F, eds). Philadelphia: Lippincott Williams & Wilkins.

Bergdahl J. 1995. Psychologic aspects of patients with symptoms presumed to be caused by electricity or visual-display units. Acta Odontol Scand 53:304-310.

Berger H. 1929. Über das Elektrenkephalogramm des Menschen. Arch Psychiatr Nervenkr 87:527-570.

Besset A, Espa F, Dauvilliers Y, Billiard M, de Seze R. 2005. No effect on cognitive function from daily mobile phone use. Bioelectromagnetics 26:102-108.

Borbély AA, Baumann F, Brandeis D, Strauch I, Lehmann D. 1981. Sleep deprivation: Effect on sleep stages and EEG power density in man. Electroencephalogr Clin Neurophysiol 51:483-493.

Borbély AA, Huber R, Graf T, Fuchs B, Gallmann E, Achermann P. 1999. Pulsed high-frequency electromagnetic field affects human sleep and sleep electroencephalogram. Neurosci Lett 275:207-210.

Braver TS, Cohen JD, Nystrom LE, Jonides J, Smith EE, Noll DC. 1997. A parametric study of prefrontal cortex involvement in human working memory. Neuroimage 5:49-62.

Braver TS, Barch DM, Kelley WM, Buckner RL, Cohen NJ, Miezin FM, et al. 2001. Direct comparison of prefrontal cortex regions engaged by working and long-term memory tasks. Neuroimage 14:48-59.

Bulpitt CJ, Fletcher AE. 1990. The measurement of quality of life in hypertensive patients: A practical approach. Br J Clin Pharmac 30:353-364.

CENELEC. 2001. Basic standard for the measurement of specific absorption rate related to human exposure to electromagnetic fields from mobile phones (300 MHz-3 GHz) (EN 50361). Belgium: European Committee for Electrotechnical Standardization.

Chavannes N, Tay R, Nikoloski N, Kuster N. 2003. Suitability of FDTD-based TCAD tools for RF design of mobile phones. IEEE Antennas Propag Mag 45:52-66.

Cooley WJ, Tukey JW. 1965. An algorithm for the machine calculation of complex Fourier series. Math Comput 19:297-301.

Coray R, Krähenbühl P, Riederer M, Stoll D, Neubauer DIG, Szentkuti B. 2002. Immissionen in Salzburg. Switzerland: BAKOM. Available: http://www.bakom.ch/dokumentation/zahlen/00545/00547/00548/index.html?lang=de [accessed 28 August 2006].

Croft R, Chandler J, Burgess A, Barry R, Williams J, Clarke A. 2002. Acute mobile phone operation affects neural function in humans. Clin Neurophysiol 113:1623-1632.

Crowell DH, Kapunial LE, Boychuk RB, Light MJ, Hodgman JE. 1982. Daytime sleep stage organization in 3-month-old-infants. Electroencephalogr Clin Neurophysiol 53:36-47.

Curcio G, Ferrara M, De Gennaro L, Cristiani R, D'Inzeo G, Bertini M. 2004. Time-course of electromagnetic field effects on human performance and tympanic temperature. Neuroreport 15:161-164.

Curcio G, Ferrara M, Moroni F, D'Inzeo G, Bertini M, De Gennaro L. 2005. Is the brain influenced by a phone call? An EEG study of resting wakefulness. Neurosci Res 53:265-270.

D'Costa H, Trueman G, Tang L, Abdel-rahman U, Abdel-rahman W, Ong K, et al. 2003. Human brain wave activity during exposure to radiofrequency field emissions from mobile phones. Australas Phys Eng Sci Med 26:162-167.

Davis H, Davis PA. 1936. Action potentials of the brain - In normal persons and in normal states of cerebral activity. Arch Neurol Psychiatry 36:1214-1224.

Dement W, Kleitman N. 1957. Cyclic variations in EEG during sleep and their relation to eye movements, body motility, and dreaming. Electroencephalogr Clin Neurophysiol 9:673-690.

Dijk DJ, Beersma DGM, Van den Hoofdakker RH. 1989. All night spectral analysis of EEG sleep in young adult and middle-aged male subjects. Neurobiol Aging 10:677-682.

Dijk DJ, Hayes B, Czeisler CA. 1993. Dynamics of electroencephalographic sleep spindles and slow wave activity in men: Effect of sleep deprivation. Brain Res 626:190-199.

Dijk DJ, Czeisler CA. 1995a. Contribution of the circadian pacemaker and the sleep homeostat to sleep propensity, sleep structure, electroencephalographic slow waves, and sleep spindle activity in humans. J Neurosci 15:3526-3538.

Dijk DJ, Roth C, Landolt HP, Werth E, Aeppli M, Achermann P, et al. 1995b. Melatonin effect on daytime sleep in men: Suppression of EEG low frequency activity and enhancement of spindle frequency activity. Neurosci Lett 201:13-16.

Durney CH, Massoudi H, Iskander MF. 1997. Radiofrequency radiation dosimetry handbook. Texas: USAF School of Aerospace Medicine, Aerospace Medical Division (AFSC), Brooks Air Force Base.

Edelstyn N, Oldershaw A. 2002. The acute effects of exposure to the electromagnetic field emitted by mobile phones on human attention. Neuroreport 13:119-121.

Eliyahu I, Luria R, Hareuveny R, Margaliot M, Meiran N, Shani G. 2006. Effects of radiofrequency radiation emitted by cellular telephones on the cognitive functions of humans. Bioelectromagnetics 27:119-126.

Ellingson RJ. 1982. Development of sleep spindle bursts during the first year of life. Sleep 5:39-46.

Endo T, Roth C, Landolt HP, Werth E, Aeschbach D, Achermann P, et al. 1998. Selective REM sleep deprivation in humans: Effects on sleep and sleep EEG. Am J Physiol 274:R1186-R1194.

Eulitz C, Ullsperger P, Freude G, Elbert T. 1998. Mobile phones modulate response patterns of human brain activity. Neuroreport 9:3229-3232.

Federal Communications Commission. 2005. Cellular telephone specific absorption rate (SAR) [accessed Dec 16, 2005].

Ferreri F, Curcio G, Pasqualetti P, De Gennaro L, Fini R, Rossini PM. 2006. Mobile phone emissions and human excitability. Ann Neurol 60:188-196.

Freude G, Ullsperger P, Eggert S, Ruppe I. 1998. Effects of microwaves emitted by cellular phones on human slow brain potentials. Bioelectromagnetics 19:384-387.

Freude G, Ullsperger P, Eggert S, Ruppe I. 2000. Microwaves emitted by cellular telephones affect human slow brain potentials. Eur J Appl Physiol 81:18-27.

Gaillard JM, Blois R. 1981. Spindle density in sleep of normal subjects. Sleep 4:385-391.

Gamboa H. 2005. http://commons.wikimedia.org/wiki/User:Hgamboa [accessed Sept 7, 2006].

Gastaut MH. 1952. Etude électrocorticographique de la réactivité des rythmes rolandiques. Rev Neurol 87:176-182.

German Federal Office for Radiation Protection. 2005. Die SAR-Werte für Handys [accessed Dec 16, 2005].

Grob A. 1995. Subjective well-being and significant life-events across the life-span. Swiss J Psychol 54:3-18.

Haarala C, Aalto S, Hautzel H, Julkunen L, Rinne JO, Laine M, et al. 2003a. Effects of a 902 MHz mobile phone on cerebral blood flow in humans: A PET study. Neuroreport 14:2019-2023.

Haarala C, Björnberg L, Ek M, Laine M, Revonsuo A, Koivisto M, et al. 2003b. Effect of a 902 MHz electromagnetic field emitted by mobile phones on human cognitive function: A replication study. Bioelectromagnetics 24:283-288.

Haarala C, Ek M, Björnberg L, Laine M, Revonsuo A, Koivisto M, et al. 2004. 902 MHz mobile phone does not affect short term memory in humans. Bioelectromagnetics 25:452-456.

Haarala C, Bergman M, Laine M, Revonsuo A, Koivisto M, Hämäläinen H. 2005. Electromagnetic field emitted by 902 MHz mobile phones shows no effects on children's cognitive function. Bioelectromagnetics (Suppl.):S144-S150.

Hamblin DL, Wood AW, Croft RJ, Stough C. 2004. Examining the effects of electromagnetic fields emitted by GSM mobile phones on human event related potentials and performance during an auditory task. Clin Neurophysiol 115:171-178.

Hampel FR. 1985. The breakdown points of the mean combined with some rejection rules. Technometrics 27:95-107.

Hermann DM, Hossmann KA. 1997. Neurological effects of microwave exposure related to mobile communication. J Neurol Sci 152:1-14.

Hess R, Akert K, Koella W. 1950. Les potentiels bioelectriques du cortex et du thalamus et leur alteration par stimulation du centre hypnique chez le chat. Rev Neurol 83:537-544.

Hietanen M, Kovala T, Hämäläinen AM. 2000. Human brain activity during exposure to radiofrequency fields emitted by cellular phones. Scand J Work Environ Health 26:87-92.

Hinrichs H, Heinze HJ. 2004. Effects of GSM electromagnetic field on the MEG during an encoding-retrieval task. Neuroreport 15:1191-1194.

Hinrichs H, Heinze HJ, Rotte M. 2005. Human sleep under the influence of a GSM 1800 electromagnetic far field. Somnology 9:185-191.

Hinrikus H, Parts M, Lass J, Tuulik V. 2004. Changes in human EEG caused by low level modulated microwave stimulation. Bioelectromagnetics 25:431-440.

Hirata A, Morita M, Shiozawa T. 2003. Temperature increase in the human head due to a dipole antenna at microwave frequencies. IEEE Trans Electromagn Compat 45:109-116.

Hirshkowitz M, Thornby JI, Karacan I. 1982. Sleep spindles - Pharmacological effects in humans. Sleep 5:85-94.

Hladký A, Musil J, Roth Z, Urban P, Blazková V. 1999. Acute effects of using a mobile phone on CNS functions. Centr Eur J Publ Hlth 7:165-167.

Holm S. 1979. A simple sequentially rejective multiple test procedure. Scand J Statist 6:65-70.

Huber R, Graf T, Cote KA, Wittmann L, Gallmann E, Matter D, et al. 2000. Exposure to pulsed high-frequency electromagnetic field during waking affects human sleep EEG. Neuroreport 11:3321-3325.

Huber R, Treyer V, Borbély AA, Schuderer J, Gottselig JM, Landolt HP, et al. 2002. Electromagnetic fields, such as those from mobile phones, alter regional cerebral blood flow and sleep and waking EEG. J Sleep Res 11:289-295.

Huber R, Schuderer J, Graf T, Jutz K, Borbély AA, Kuster N, et al. 2003. Radio frequency electromagnetic field exposure in humans: Estimation of SAR distribution in the brain, effects on sleep and heart rate. Bioelectromagnetics 24:262-276.

Huber R, Treyer V, Schuderer J, Berthold T, Buck A, Kuster N, et al. 2005. Exposure to pulse-modulated radio frequency electromagnetic fields affects regional cerebral blood flow. Eur J Neurosci 21:1000-1006.

Hutter HP, Moshammer H, Wallner P, Kundi M. 2006. Subjective symptoms, sleeping problems, and cognitive performance in subjects living near mobile phone base stations. Occup Environ Med 63:307-313.

Hyland GJ. 2000. Physics and biology of mobile telephony. Lancet 356:1833-1836.

ICNIRP. 1998. Guidelines for limiting exposure to time-varying electric, magnetic, and electromagnetic fields (up to 300 GHz). Health Phys 74:494-522.

IEEE. 2002. IEEE recommended practice for measurements and computations of radio frequency electromagnetic fields with respect to human exposure to such fields, 100 kHz to 300 GHz (Std C95.3). New York: The Institute of Electrical and Electronics Engineers, Inc.

IEEE. 2002. IEEE standard for safety levels with respect to human exposure to electromagnetic fields, 0-3 kHz (Std C95.6). New York: The Institute of Electrical and Electronics Engineers, Inc.

IEEE. 2005. IEEE standard for safety levels with respect to human exposure to radio frequency electromagnetic fields, 3 kHz to 300 GHz (Std C95.1). New York: The Institute of Electrical and Electronics Engineers, Inc.

Jaeggi SM, Seewer R, Nirkko AC, Eckstein D, Schroth G, Groner R, et al. 2003. Does excessive memory load attenuate activation in the prefrontal cortex? Load-dependent processing in single and dual tasks: fFnctional magnetic resonance imaging study. Neuroimage 19:210-225.

Jasper HH. 1958. Report on the committee on methods of clinical examination in electroencephalography. Electroencephalogr Clin Neurophysiol 10:370-375.

Jech R, Sonka K, Ruzicka E, Nebuzelsky A, Böhm J, Juklickova M, et al. 2001. Electromagnetic field of mobile phones affects visual event related potential in patients with narcolepsy. Bioelectromagnetics 22:519-528.

Jenni OG, Borbély AA, Achermann P. 2004. Development of the nocturnal sleep electroencephalogram in human infants. Am J Physiol Regul Integr Comp Physiol 286:R528-R538.

Jobert M, Poiseau E, Jähnig P, Schulz H, Kubicki S. 1992. Topographical analysis of sleep spindle activity. Neuropsychobiology 26:210-217.

Johnson Liakouris AG. 1998. Radiofrequency (RF) sickness in the Lilienfeld study: An effect of modulated microwaves? Arch Environ Health 53:236-238.

Jonides J, Schumacher EH, Smith EE, Lauber EJ, Awh E, Minoshima S, et al. 1997. Verbal working memory load affects regional brain activation as measured by PET. J Cogn Neurosci 9:462-475.

Kainz W, Christ A, Kellom T, Seidman S, Nikoloski N, Beard B, et al. 2005. Dosimetric comparison of the specific anthropomorphic mannequin (SAM) to 14 anatomical head models using a novel definition for the mobile phone positioning. Phys Med Biol 50:3423-3445.

Kandel ER, Schwartz JH, Jessell TM. 2000. Principles of neural science. New York: McGraw-Hill.

Keetley V, Wood AW, Spong J, Stough C. 2006. Neuropsychological sequelae of digital mobile phone exposure in humans. Neuropsychologia 44:1843-1848.

Klimesch W. 1997. EEG-alpha rhythms and memory processes. Int J Psychophysiol 26:319-340.

Klimesch W. 1999. EEG alpha and theta oscillations reflect cognitive and memory performance: A review and analysis. Brain Res Rev 29:169-195.

Klimesch W, Doppelmayr M, Schwaiger J, Auinger P, Winkler Th. 1999. 'Paradoxical' alpha synchronization in a memory task. Cogn Brain Res 7:493-501.

Koivisto M, Krause CM, Revonsuo A, Laine M, Hämäläinen H. 2000a. The effects of electromagnetic field emitted by GSM phones on working memory. Neuroreport 11:1641-1643.

Koivisto M, Revonsuo A, Krause C, Haarala C, Sillanmäki L, Laine M, et al. 2000b. Effects of 902 MHz electromagnetic field emitted by cellular telephones on response times in humans. Neuroreport 11:413-415.

Kramarenko AV, Tan U. 2003. Effects of high-frequency electromagnetic fields on human EEG: A brain mapping study. Int J Neurosci 113:1007-1019.

Krause CM, Sillanmäki L, Koivisto M, Häggqvist A, Saarela C, Revonsuo A, et al. 2000a. Effects of electromagnetic field emitted by cellular phones on the EEG during a memory task. Neuroreport 11:761-764.

Krause CM, Sillanmäki L, Koivisto M, Häggqvist A, Saarela C, Revonsuo A, et al. 2000b. Effects of electromagnetic fields emitted by cellular phones on the electroencephalogram during a visual working memory task. Int J Radiat Biol 76:1659-1667.

Krause CM, Haarala C, Sillanmäki L, Koivisto M, Alanko K, Revonsuo A, et al. 2004. Effects of electromagnetic field emitted by cellular phones on the EEG during an auditory memory task: A double blind replication study. Bioelectromagnetics 25:33-40.

Kuster N, Balzano Q. 1992. Energy absorption mechanism by biological bodies in the near field of dipole antennas above 300 MHz. IEEE Trans Veh Technol 41:17-23.

Kuster N, Kästle R, Schmid T. 1997. Dosimetric evaluation of handheld mobile communications equipment with known precision. IEICE Trans Commun E80-B:645-651.

Kuster N, Schönborn F. 2000. Recommended minimal requirements and development guidelines for exposure setups of bio-experiments addressing the health risk concern of wireless communications. Bioelectromagnetics 21:508-514.

Kuster N, Schuderer J, Christ A, Futter P, Ebert S. 2004. Guidance for exposure design of human studies addressing health risk evaluations of mobile phones. Bioelectromagnetics 25:524-529.

Landolt HP, Dijk DJ, Achermann P, Borbély AA. 1996. Effect of age on the sleep EEG: Slow-wave activity and spindle frequency activity in young and middle-aged men. Brain Res 738:205-212.

Lass J, Tuulik V, Ferenets R, Riisalo R, Hinrikus H. 2002. Effects of 7 Hz-modulated 450 MHz electromagnetic radiation on human performance in visual memory tasks. Int J Radiat Biol 78:937-944.

Lebedeva NN, Sulimov AV, Sulimova OP, Kotrovskaya TI, Gailus T. 2000. Cellular phone electromagnetic field effects on bioelectric activity of human brain. Crit Rev Biomed Eng 28:323-337.

Lebedeva NN, Sulimov AV, Sulimova OP, Korotkovskaya TI, Gailus T. 2001. Investigation of brain potentials in sleeping humans exposed to the electromagnetic field of mobile phones. Crit Rev Biomed Eng 29:125-133.

Lee TM, Ho SM, Tsang LY, Yang SH, Li LS, Chan CC, et al. 2001. Effect on human attention of exposure to the electromagnetic field emitted by mobile phones. Neuroreport 12:729-731.

Lee TMC, Lam PK, Yee LTS, Chan CCH. 2003. The effect of the duration of exposure to the electromagnetic field emitted by mobile phones on human attention. Neuroreport 14:1361-1364.

Leitgeb N, Schröttner J. 2003. Electrosensibility and electromagnetic hypersensitivity. Bioelectromagnetics 24:387-394.

Loomis AL, Newton Harvey E, Hobart G. 1935. Potential rhythms of the cerebral cortex during sleep. Science 81:597-598.

Lopes da Silva F. 2005. Event related potentials: Methodology and quantification. In: Electroencephalography: Basic principles, clinical applications, and related fields (Niedermeyer E, Lopes da Silva F, eds). Philadelphia: Lippincott Williams & Wilkins.

Loughran SP, Wood AW, Barton JM, Croft RJ, Thompson B, Stough C. 2005. The effect of electromagnetic fields emitted by mobile phones on human sleep. Neuroreport 16:1973-1976.

Louis J, Zhang JX, Revol M, Debilly G, Challamel MJ. 1992. Ontogeny of nocturnal organization of sleep spindles - A longitudinal study during the first 6 months of life. Electroencephalogr Clin Neurophysiol 83:289-296.

Mann K, Röschke J. 1996. Effects of pulsed high-frequency electromagnetic fields on human sleep. Neuropsychobiology 33:41-47.

McCormick DA. 1992. Neurotransmitter actions in the thalamus and cerebral cortex and their role in neuromodulation of thalamocortical activity. Prog Neurobiol 39:337-388.

Moruzzi G, Magoun HW. 1949. Brain stem and EEG activation. Electroencephalogr Clin Neurophysiol 1:455-473.

Moulder JE. 1998. Power-frequency fields and cancer. Crit Rev Biomed Eng 26:1-116.

Müller B, Basler HD. 1993. Kurzfragebogen zur aktuellen Beanspruchung (KAB). Weinheim: Beltz.

National Institute of Environmental Health Sciences - NIEHS Working Group Report. 1998. Assessment of health effects from exposure to power-line frequency electric and magnetic fields. Minnesota: National Institute of Environmental Health Sciences/National Institutes of Health.

Navarro EA, Segura J, Portolés M, Gómez-Perretta C. 2003. The microwave syndrome: A preliminary study in Spain. Electromagn Biol Med 22:161-169.

Nicolas A, Petit D, Rompré S, Montplaisir J. 2001. Sleep spindle characteristics in healthy subjects of different age groups. Clin Neurophysiol 112:521-527.

Niedermeyer E, Krauss GL, Peyser CE. 1989. The electroencephalogram and mental activation. Clin Electroencephalogr 20:215-227.

Niedermeyer E. 2005. The normal EEG of the waking adult. In: Electroencephalography: Basic principles, clinical applications, and related fields (Niedermeyer E, Lopes da Silva F, eds). Philadelphia: Lippincott Williams & Wilkins.

Noachtar S, Binnie C, Ebersole J, Mauguière F, Sakamoto A, Westmoreland B. 1999. A glossary of terms most commonly used by clinical electroencephalographers and proposal for the report form for the EEG findings. In: Recommendations for the practice of clinical neurophysiology: Guidelines of the International Federation of Clinical Neurophysiology (Deuschl G, Eisen A, eds). Amsterdam: Elsevier.

Oldfield RC. 1971. The assessment and analysis of handedness: The Edinburgh inventory. Neuropsychologia 9:97-113.

Papageorgiou CC, Nanou ED, Tsiafakis VG, Capsalis CN, Rabavilas AD. 2004. Gender related differences on the EEG during a simulated mobile phone signal. Neuroreport 15:2557-2560.

Pasche B, Erman M, Hayduk R, Mitler MM, Reite M, Higgs L, et al. 1996. Effects of low energy emission therapy in chronic psychophysiological insomnia. Sleep 19:327-336.

Pfurtscheller G, Aranibar A. 1977. Event related cortical desynchronization detected by power measurements of scalp EEG. Electroencephalogr Clin Neurophysiol 42:817-826.

Pfurtscheller G. 1991. EEG rhythms - Event related desynchronization and synchronization. In: Rhythms in physiological systems (Haken H, Koepchen HP, eds). Berlin Heidelberg: Springer-Verlag.

Preece AW, Wesnes KA, Iwi GR. 1998. The effect of a 50 Hz magnetic field on cognitive function in humans. Int J Radiat Biol 74:463-470.

Preece AW, Iwi G, Davies-Smith A, Wesnes K, Butler S, Lim E, et al. 1999. Effect of a 915-MHz simulated mobile phone signal on cognitive function in man. Int J Radiat Biol 75:447-456.

Preece AW, Goodfellow S, Wright MG, Butler SR, Dunn EJ, Johnson Y, et al. 2005. Effect of 902 MHz mobile phone transmission on cognitive function in children. Bioelectromagnetics 26 (Suppl.):S138-S143.

Principe JC, Smith JR. 1982. Sleep spindle characteristics as a function of age. Sleep 5:73-84.

Rechtschaffen A, Kales A. 1968. A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects. Bethesda, Maryland: National Institutes of Health.

Regel SJ, Negovetic S, Röösli M, Berdiñas V, Schuderer J, Huss A, et al. 2006. UMTS base station-like exposure, well-being, and cognitive performance. Environ Health Perspect 114:1270-1275.

Reiser H, Dimpfel W, Schober F. 1995. The influence of electromagnetic fields on human brain activity. Eur J Med Res 1:27-32.

Rétey JV, Adam M, Gottselig JM, Khatami R, Dürr R, Achermann P, Landolt HP. 2006. Adenosinergic mechanisms contribute to individual differences in sleep deprivation-induced changes in neurobehavioral function and brain rhythmic activity. J Neurosci 26:10472-10479.

Röösli M, Moser M, Baldinini Y, Meier M, Braun-Fahrländer C. 2004. Symptoms of ill health ascribed to electromagnetic field exposure - A questionnaire survey. Int J Hyg Environ Health 207:141-150.

Röschke J, Mann K. 1997. No short-term effects of digital mobile radio telephone on the awake human electroencephalogram. Bioelectromagnetics 18:172-176.

Rosenthal R. 1968. Self-fulfilling prophecy. Psychol Today 2:44-51.

Rubin GJ, Das Munshi J, Wessely S. 2005. Electromagnetic hypersensitivity: A systematic review of provocation studies. Psychosom Med 67:224-232.

Rubin GJ, Das Munshi J, Wessely S. 2006. A systematic review of treatments for electromagnetic hypersensitivity. Psychother Psychosom 75:12-18.

Russo R, Fox E, Cinel C, Boldini A, Defeyter MA, Mirshekar-Syahkal D, et al. 2006. Does acute exposure to mobile phones affect human attention? Bioelectromagnetics 27:215-220.

Santini R, Santini P, Le Ruz P, Danze JM, Seigne M. 2003. Survey study of people living in the vicinity of cellular phone base stations. Electromagn Biol Med 22:41-49.

Schmid G, Sauter C, Stepansky R, Lobentanz IS, Zeitlhofer J. 2005. No influence on selected parameters of human visual perception of 1970 MHz UMTS-like exposure. Bioelectromagnetics 26:243-250.

Schmid T, Egger O, Kuster N. 1996. Automated E-field scanning system for dosimetric assessments. IEEE Trans Microw Theory Tech 44:105-113.

Schmidt RF, Thews G. 2000. Physiologie des Menschen. Berlin: Springer.

Seitz H, Stinner D, Eikmann T, Herr C, Röösli M. 2005. Electromagnetic hypersensitivity (EHS) and subjective health complaints associated with electromagnetic fields of mobile phone communication - A literature review published between 2000 and 2004. Sci Total Environ 349:45-55.

Smythe JW, Costall B. 2003. Mobile phone use facilitates memory in male, but not female subjects. Neuroreport 14:243-246.

Steriade M, Datta S, Paré D, Oakson G, Curró Dossi RC. 1990. Neuronal activities in brain-stem cholinergic nuclei related to tonic activation processes in thalamocortical systems. J Neurosci 10:2541-2559.

Steriade M, McCormick DA, Sejnowski TJ. 1993a. Thalamocortical oscillations in the sleeping and aroused brain. Science 262:679-685.

Steriade M, Nuñez A, Amzica F. 1993b. A novel slow (<1 Hz) oscillation of neocortical neurons in vivo: Depolarizing and hyperpolarizing components. J Neurosci 13:3252-3265.

Steriade M. 2003a. The corticothalamic system in sleep. Front Biosci 8:d878-d899.

Steriade M, Timofeev I. 2003b. Neuronal plasticity in thalamocortical networks during sleep and waking oscillations. Neuron 37:563-576.

Storm van Leeuwen W, Bekkering IDH. 1958. Some results obtained with the EEG-Spectrograph. Electroencephalogr Clin Neurophysiol 10:563-570.

Surwillo WW. 1961. Frequency of alpha rhythm, reaction time and age. Nature 191:823-824.

Tanguay PE, Ornitz EM, Kaplan A, Bozzo ES. 1975. Evolution of sleep spindles in childhood. Electroencephalogr Clin Neurophysiol 38:175-181.

Tukey JW, Ciminera JL, Heyse JF. 1985. Testing the statistical certainty of a response to increasing doses of a drug. Biometrics 41:295-301.

Uchida S, Maloney T, March JD, Azari R, Feinberg I. 1991. Sigma 12-15 Hz and delta 0.3-3 Hz EEG oscillate reciprocally within NREM sleep. Brain Res Bull 27:93-96.

Urban P, Lukás E, Roth Z. 1998. Does acute exposure to the electromagnetic field emitted by a mobile phone influence visual evoked potentials? A pilot study. Centr Eur J Publ Hlth 6:288-290.

van Beijsterveldt CEM, Molenaar PCM, De Geus EJC, Boomsma DI. 1996. Heritability of human brain functioning as assessed by electroencephalography. Am J Hum Genet 58:562-573.

von Economo C. 1917. Encephalitis lethargica. Wien Klin Wochen 30:581-585.

von Klitzing L. 1995. Low-frequency pulsed electromagnetic fields influence EEG of man. Phys Med XI:77-80.

Wagner P, Röschke J, Mann K, Hiller W, Frank C. 1998. Human sleep under the influence of pulsed radiofrequency electromagnetic fields: A polysomnographic study using standardized conditions. Bioelectromagnetics 19:199-202.

Wagner P, Röschke J, Mann K, Fell J, Hiller W, Frank C, et al. 2000. Human sleep EEG under the influence of pulsed radio frequency electromagnetic fields. Results from polysomnographies using submaximal high power flux densities. Neuropsychobiology 42:207-212.

Wang JQ, Fujiwara O. 1999. FDTD computation of temperature rise in the human head for portable telephones. IEEE Trans Microw Theory Tech 47:1528-1534.

Werth E, Achermann P, Dijk DJ, Borbély AA. 1997. Spindle frequency activity in the sleep EEG: Individual differences and topographic distribution. Electroencephalogr Clin Neurophysiol 103:535-542.

Wiart J, Dale C, Bosisio AV, Le Cornec A. 2000. Analysis of the influence of the power control and discontinuous transmission on RF exposure with GSM mobile phones. IEEE Trans Electromagn Compat 42:376-385.

Wieneke GH, Deinema CHA, Spoelstra P, Vanleeuwen WS, Versteeg H. 1980. Normative spectral data on alpha rhythm in male adults. Electroencephalogr Clin Neurophysiol 49:636-645.

World Health Organization. 2000. Electromagnetic fields and public health: Mobile telephones and their base stations. Fact Sheet No 193, Available: http://www.who.int/mediacentre/factsheets/fs193/en/ [accessed 18 August 2006].

World Health Organization. 2005. Electromagnetic fields and public health: Electromagnetic hypersensitivity. Fact Sheet No 296, Available: http://www.who.int/mediacentre/factsheets/fs296/en/ [accessed 18 August 2006].

Yuasa K, Arai N, Okabe S, Tarusawa Y, Nojima T, Hanajima R, et al. 2006. Effects of thirty minutes mobile phone use on the human sensory cortex. Clin Neurophysiol 117:900-905.

Ziskin MC. 2002. Electromagnetic hypersensitivity - A COMAR technical information statement. IEEE Eng Med Biol Mag 21:173-175.

Zwamborn APM, Vossen SHJA, van Leersum BJAM, Ouwens MA, Mäkel WN. 2003. Effects of global communication system radio frequency fields on well-being and cognitive functions of human subjects with and without subjective complaints FEL-03-C148. Netherlands: TNO Physics and Electronics Laboratory. Available: http://home.tiscali.be/milieugezondheid/dossiers/gsm/TNO_rapport_Nederland_sept_2003.pdf [accessed 19 April 2006].

APPENDIX

Four cognitive tasks previously applied in RF-EMF research were selected to investigate the effects of EMF radiation on brain functioning: the SRT, CRT, N-back and VSAT (Koivisto et al. 2000a; Koivisto et al. 2000b; Preece et al. 1998; 1999; Zwamborn et al. 2003). In all tasks, black stimuli were presented in a gray box (SRT: 4.2 x 4.5 cm; CRT: 5.9 x 4.5 cm; N-back: 4.8 x 3.4 cm; VSAT: 10.0 x 7.5 cm (length x height)) in the middle of a black screen. The tasks were always applied in a fixed order (SRT, CRT, 1-, 2-, 3-back, VSAT) to ensure the same amount of time between the tasks from the first to the second series. Subjects were instructed to respond as quickly and as accurately as possible by pressing various buttons corresponding to the respective targets on a response box.

Whereas the SRT, the CRT and the VSAT mainly constitute typical tasks to measure selective and divided attention and speed of decision making, the N-back task is widely used in experiments tackling working memory performance (e.g., Braver et al. 2001; Jaeggi et al. 2003). In this respect, Braver et al. (1997) found a linear relationship between the activation of dorsolateral and left inferior regions of the prefrontal cortex and memory load. Jonides et al. (1997) showed that an increase in task difficulty accomplished by varying the value of “n” resulted in an increasing magnitudes of brain activation in a large number of sites that together have been identified with verbal working-memory processes.

Simple Reaction Time Task (SRT)

In the SRT, a ”0” appeared on screen until the subjects pressed the corresponding “0” button with the right index finger. The next stimulus appeared with a random delay of 1000-4000 ms (in steps of 500 ms). A total of 42 targets per session was presented. Completion of the task took about 2-3 min.

Two-choice Reaction Time Task (CRT)

In the CRT, either "*JA"* (yes) or "*NEIN"* (no) appeared on the screen and subjects had to press the corresponding “J” button with their right index finger and the “N” button with their right middle finger, respectively. The next stimulus appeared with a random delay of 1000-3500 ms (in steps of 500 ms). A total of 24 “yes” and 24 “no” targets per session was presented. Completion of the task took about 2-3 min.

N-back Task (N-back)

In the N-back task the stimuli were single consonants presented in a random order with varying letter case. Three different memory workload levels were used. In the 1-back task, the target was any letter presented 1 trial back (i.e., G-g). In the 2-back and 3-back task, the target was any letter presented two trials (e.g., G-c-g) or three trials back (e.g., G-c-h-g). Each letter was displayed until the subject responded but maximally for 2000 ms (interstimulus interval 1000 ms). Subjects had to respond to the targets (same letter) with their right index finger, and to non-targets (different letters) with their right middle finger. Each task (1-back, 2-back, and 3-back) consisted of 24 targets and 56 non-targets, preceded by a practice block without feedback including three targets and seven non-targets. Completion of the task took about 9-12 min.

Visual Selective Attention Task (VSAT)

In the VSAT a randomized combination of four letters and/or crosses arranged in a grey square was presented on the screen. The targets were the letters “U” and “F” appearing on the diagonal from upper left to lower right. Subjects were instructed to press the “J” button with their right index finger if one or both targets appeared and the “N” button with their right middle finger if no target was presented. Stimuli were displayed until the subject responded but maximally for 2000 ms (interstimulus interval 500 ms). Each session consisted of 16 targets and 64 non-targets, preceded by practice block with feedback including 3 targets and 7 non-targets. Completion of the VSAT took about 2-4 min. Completion of all tasks in one series took 15-20 min.

FIGURES AND TABLES

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Studies and Training Periods

2002 - 2006	Doctoral student at the Section of Psychopharmacology and Sleep Research, Institute of Pharmacology and Toxicology, University of Zürich, Switzerland
2003 – 2006	Participation in the “Ph.D. Program in Neuroscience” at the Neuroscience Center Zürich, Switzerland
2002	Research assistant at the Human Behavioral Pharmacology Laboratory, Department of Psychiatry, University of Chicago, Illinois, USA (3 months)
2001	Graduation at the Heinrich-Heine-University Düsseldorf, Germany
1997	Internship at the Children’s’ Psychiatry in Bochum, Germany (2 months)
1997	Internship at the neuropsychological section of the Neurology Department, Rheinische Landeskliniken Düsseldorf, Germany (2 months)
1994	Start as a psychology graduate student at the Heinrich-Heine-University Düsseldorf, Germany
1985 – 1994	High school, Abitur (Oberhausen, Germany)

List of Publications

Regel SJ, Tinguely G, Schuderer J, Adam M, Kuster N, Landolt HP, and Achermann P. Pulsed radio frequency electromagnetic fields: Dose-dependent effects on sleep, the sleep EEG and cognitive performance (in preparation).

Regel SJ, Gottselig JM, Schuderer J, Tinguely G, Rétey JV, Kuster N, Landolt HP, and Achermann P. Pulsed radio frequency radiation affects cognitive performance and the waking EEG (submitted).

Regel SJ, Negovetic S, Röösli M, Berdiñas V, Schuderer J, Huss A, Lott U, Kuster N and Achermann P. 2006. UMTS base station-like exposure, well-being and cognitive performance. Environ Health Perspect 114:1270-1275.

Hofer-Tinguely G, Achermann P, Landolt HP, Regel SJ, Rétey JV, Dürr R, Borbély AA and Gottselig JM. 2005. Sleep inertia: Performance changes after sleep, rest and activity. Cogn Brain Res 22:323-331.

Gottselig JM, Hofer-Tinguely G, Borbély AA, Regel SJ, Landolt HP, Rétey JV and Achermann P. 2004. Sleep and rest facilitate auditory learning. Neuroscience 127:557-561.

Schneider F, Habel U, Volkmann J, Regel S, Kornischka J, Sturm V, Freund JH. 2003. Deep brain stimulation of the subthalamic nucleus enhances emotional processing in Parkinson disease. Arch Gen Psychiatry 60:296-302.

Congresses & Meetings

Symposium of the Neuroscience Center Zürich (ZNZ), Zürich, October 2006 (Poster)

Annual Meeting of the Center for Integrative Human Physiology (CHIP), Zürich, September 2006 (Poster)

Annual Meeting of the European Sleep Research Society (ESRS), Innsbruck, Austria, September 2006 (Poster)

Annual Meeting of the Swiss Society for Sleep research, Sleep medicine and Chronobiology (SGSSC), Tschugg, May 2006

Opening Symposium of the Center for Integrative Human Physiology CIHP), Zürich, September 2005 (Poster)

Annual Meeting of the Swiss Society for Sleep research, Sleep medicine and Chronobiology (SGSSC), Luzern, April 2005

Symposium of the Neuroscience Center Zürich (ZNZ), Zürich, October 2005 (Poster)

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Annual Meeting of the Swiss Society for Sleep research, Sleep medicine and Chronobiology (SGSSC), Basel, December 2004 (Poster)

Symposium of the Neuroscience Center Zürich (ZNZ), Zürich, October 2004 (Poster, Data Blitz)

Annual Meeting of the European Sleep Research Society (ESRS), Prague, September 2004 (Poster)

Annual Meeting of the Swiss Society for Neuroscience (SSN), Lausanne, January 2004 (Poster, Data Blitz)

Symposium of the Neuroscience Center Zürich (ZNZ), Zürich, October 2003 (Co-Author/Poster)

Annual Meeting of the Associated Professional Sleep Societies (APSS), Chicago, June 2003 (Co-Author/Poster)

Symposium of the Neuroscience Center Zürich (ZNZ), Zürich, October 2002

Congress of the German Society for Biological Psychiatry (DGBP), Düsseldorf, October 2002 (Co-Author/Poster)